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<input type="checkbox"/>	L5	simulect or zevalin and (human adj monoclonal) and (anti adj cd25) and (anti adj tac) and antibody	69
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Limits: **Publication Date to 2003/11/14**

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#33	Search simulect or zevalin Limits: Publication Date to 2003/11/14	13:13:55	275
#32	Search simulect and zevalin Limits: Publication Date to 2003/11/14	13:12:37	1
#30	Search (human monoclonal antibody) and tac and cd25 Limits: Publication Date to 2003/11/14	12:42:37	404
#29	Search (human monoclonal antibody) and tac Limits: Publication Date to 2003/11/14	12:42:31	704
#26	Search (human monoclonal antibody) Limits: Publication Date to 2003/11/14	12:42:25	108014
#28	Search (human monoclonal) Limits: Publication Date to 2003/11/14	12:42:14	119334
#25	Search (human anti-Tac antibody) and cd25 and IgG1 Limits: Publication Date to 2003/11/14	12:38:05	23
#23	Search (human anti-Tac antibody) and cd25 Limits: Publication Date to 2003/11/14	12:37:05	350
#21	Search (human anti-Tac antibody) Limits: Publication Date to 2003/11/14	12:36:11	503
#20	Search human anti-Tac antibody Limits: Publication Date to 2003/11/14	12:36:01	503

<u>#18</u> Search CD25 antibody and (human IgG1) and IL2 binding Limits: Publication Date to 2003/11/14	12:34:53	8
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<u>#6</u> Search (human monoclonal) and CD25 and Limits: Publication Date to 2003/11/14	12:22:35	<u>2378</u>
<u>#5</u> Search human monoclonal and CD25 Limits: Publication Date to 2003/11/14	12:21:10	<u>2378</u>
<u>#4</u> Search A27/Jk5 Limits: Publication Date to 2003/11/14	12:20:19	0
<u>#3</u> Search A27/Jk4 Limits: Publication Date to 2003/11/14	12:20:12	0
<u>#2</u> Search Vh1-69/JH5b Limits: Publication Date to 2003/11/14	12:19:54	0
<u>#1</u> Search Vh1-69/JH4b Limits: Publication Date to 2003/11/14	12:19:40	<u>0</u>

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=> file caplus, bioeng, biotechno, biotechds, esbiobase
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=> (human monoclonal antibody)
(HUMAN IS NOT A RECOGNIZED COMMAND
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=> s (human monoclonal antibody)
L1 7262 (HUMAN MONOCLONAL ANTIBODY)

=> s (cd25 or tac or (il-2 receptor))
L2 31221 (CD25 OR TAC OR (IL-2 RECEPTOR))

=> s l1 and l2
L3 45 L1 AND L2

=> duplicate remove l3
DUPLICATE PREFERENCE IS 'CAPLUS, BIOTECHNO, BIOTECHDS, ESBIOBASE'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L3
L4 42 DUPLICATE REMOVE L3 (3 DUPLICATES REMOVED)

=> s (il-2 binding)
L5 658 (IL-2 BINDING)

=> duplicate remove l5
DUPLICATE PREFERENCE IS 'CAPLUS, BIOENG, BIOTECHNO, BIOTECHDS, ESBIOBASE'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L5
L6 385 DUPLICATE REMOVE L5 (273 DUPLICATES REMOVED)

=>

=> d his

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FILE 'CAPLUS, BIOENG, BIOTECHNO, BIOTECHDS, ESBIOBASE' ENTERED AT
14:42:08 ON 23 AUG 2006

L1 7262 S (HUMAN MONOCLONAL ANTIBODY)
L2 31221 S (CD25 OR TAC OR (IL-2 RECEPTOR))
L3 45 S L1 AND L2
L4 42 DUPLICATE REMOVE L3 (3 DUPLICATES REMOVED)
L5 658 S (IL-2 BINDING)
L6 385 DUPLICATE REMOVE L5 (273 DUPLICATES REMOVED)

=> s l4 and l6
L7 2 L4 AND L6

=> duplicate remove l7
PROCESSING COMPLETED FOR L7
L8 2 DUPLICATE REMOVE L7 (0 DUPLICATES REMOVED)

=> d l8 bib abs 1-2

L8 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1991:677524 CAPLUS
DN 115:277524
TI Monoclonal antibodies defining distinct epitopes of the human IL-2 receptor β chain and their differential effects on IL-2 responses
AU Ohbo, Kazuyuki; Takeshita, Toshikazu; Asao, Hironobu; Kurahayashi, Yumiyo; Tada, Kotaro; Mori, Hisashi; Hatakeyama, Masanori; Taniguchi, Tadatsugu; Sugamura, Kazuo
CS Sch. Med., Tohoku Univ., Sendai, 980, Japan
SO Journal of Immunological Methods (1991), 142(1), 61-72
CODEN: JIMMBG; ISSN: 0022-1759
DT Journal
LA English
AB Five new monoclonal antibodies (mAbs) were prepared which specifically immunoppt. the human interleukin-2 receptor β chain (IL-2R β). One of them, TU30, recognizes the intracytoplasmic serine-rich region of IL-2R β that is critical for IL-2 signal transduction. The others, TU12, TU21, TU23, and TU25, completely inhibit IL-2 binding, as does the previously characterized TU27. However, reciprocal binding competition assays show that the epitopes recognized by the individual mAbs are different from each other. The mAbs inhibit the growth of IL-2-dependent cells. The magnitude of their inhibitory effects is dependent on not only the affinities of the mAbs for IL-2R β but also upon the number of IL-2R α subunits expressed on IL-2-dependent cells. These mAbs should be useful in studying the structure and function of the IL-2R.

L8 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1986:531919 CAPLUS
DN 105:131919
TI High- and low-affinity interleukin 2 receptors: distinctive effects of monoclonal antibodies
AU Fujii, Masahiro; Sugamura, Kazuo; Nakai, Shinichi; Tanaka, Yuetsu; Tozawa, Hideki; Hinuma, Yorio
CS Inst. Virus Res., Kyoto Univ., Kyoto, 606, Japan
SO Journal of Immunology (1986), 137(5), 1552-6
CODEN: JOIMA3; ISSN: 0022-1767
DT Journal
LA English
AB The effects of monoclonal antibodies to human interleukin 2 (IL 2) receptor on the binding of 125I-labeled IL 2 to high- and low-affinity receptors were examined by Scatchard plot anal. Two of these monoclonal antibodies, H1E1 and H-47, reduced the IL 2-binding affinity of high-affinity receptors from a dissociation constant Kd of 14-20 pM to a Kd of 110-140 pM, but slightly raised that of low-affinity receptors. These 2 antibodies scarcely affected the nos. of high- and low-affinity receptors. On the other hand, H-31 completely blocked IL 2 binding to both high- and low-affinity receptors, and H-A26 slightly reduced the affinities of both high- and low-affinity receptors, from 17 pM to 28 pM and from 28 nM to 54 nM, resp. H-48 had little effect on IL 2 binding to high- or low-affinity receptors. By use of these monoclonal antibodies, the inhibitory effect of IL 2 on growth of a human T-lymphotropic virus type-immortalized T cell line was demonstrated to be transmitted from high-affinity, but not low-affinity, receptors.

=> s xenomouse and cd25
L9 0 XENOMOUSE AND CD25

=> d his

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FILE 'CAPLUS, BIOENG, BIOTECHNO, BIOTECHDS, ESBIOBASE' ENTERED AT
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L1 7262 S (HUMAN MONOCLONAL ANTIBODY)
L2 31221 S (CD25 OR TAC OR (IL-2 RECEPTOR))
L3 45 S L1 AND L2
L4 42 DUPLICATE REMOVE L3 (3 DUPLICATES REMOVED)
L5 658 S (IL-2 BINDING)
L6 385 DUPLICATE REMOVE L5 (273 DUPLICATES REMOVED)
L7 2 S L4 AND L6
L8 2 DUPLICATE REMOVE L7 (0 DUPLICATES REMOVED)
L9 0 S XENOMOUSE AND CD25

=> d l4 bib abs 1-42

L4 ANSWER 1 OF 42 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2006-13769 BIOTECHDS
TI Producing interleukin-22 receptor (IL-22RA) antibody, useful in treatment
of e.g. inflammatory and autoimmune disorders, by inoculating animal with
IL-22RA polypeptide to elicit immune response, and isolating antibody
from animal;
recombinant protein for use in monoclonal antibody, humanized antibody
production for use in disease diagnosis and therapy
AU XU W; KINDSVOGEL W R; CHANDRASEKHER Y A; DILLON S R; LEHNER J M; SIADAK A
W; SIVAKUMAR P V; MOORE M D
PA ZYMOGENETICS INC
PI WO 2006047249 4 May 2006
AI WO 2005-US37821 21 Oct 2005
PRAI US 2004-621553 22 Oct 2004; US 2004-621553 22 Oct 2004
DT Patent
LA English
OS WPI: 2006-343004 [35]
AN 2006-13769 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Producing (M1) antibody to polypeptide, involves inoculating
animal with a fully defined 574 amino acid (SEQ ID Number 2) sequence given
in the specification, from amino acid number 49 (Val)-amino acid number
62 (Cys) or a fully defined 211 amino acid (SEQ ID Number 3) sequence given
in the specification, and isolating antibody binding interleukin (IL)-22
receptor (IL-22RA) polypeptide and reducing activity of either IL-20 or
IL-22, from animal.
DETAILED DESCRIPTION - Producing (M1) an antibody to a polypeptide,
involves: (i) inoculating an animal with a polypeptide chosen from: (a) a
polypeptide consisting of a fully defined 211 amino acid (SEQ ID Number 3)
sequence given in the specification, from amino acid number 1 (Pro)-amino
acid number 6 (Asp); from amino acid number 26 (Ser)-amino acid number 32
(Pro); from amino acid number 41 (Lys)-amino acid number 47 (Asp); from
amino acid number 41 (Lys)-amino acid number 62 (Cys); from amino acid
number 84 (Ala)-amino acid number 97 (Ser); from amino acid number 103
(Thr)-amino acid number 108 (Asp); from amino acid number 130 (Arg)-amino
acid number 135 (His); from amino acid number 164 (Gly)-amino acid number
166 (Lys); from amino acid number 175 (Tyr)-amino acid number 179 (Glu);
from amino acid number 193 (Lys)-amino acid number 196 (Ala); or from
amino acid number 203 (Lys)-amino acid number 209 (Thr), (b) a
polypeptide consisting of a fully defined 574 amino acid (SEQ ID Number 2)
sequence given in the specification, from amino acid number 49
(Val)-amino acid number 62 (Cys), and (c) a polypeptide consisting of SEQ
ID Number 3 or comprising a fully defined 541 amino acid (SEQ ID Number 4)

sequence given in the specification, where the polypeptide elicits an immune response in the animal to produce the antibody; and (ii) isolating the antibody from the animal, where the antibody specifically binds to an interleukin (IL)-22 receptor (IL-22RA) polypeptide (SEQ ID Number 2 or 3), and reduces the activity of either IL-20 having a fully defined 176 amino acid (SEQ ID Number 8) sequence given in the specification, or IL-22 having a fully defined 179 amino acid (SEQ ID Number 6) sequence given in the specification. INDEPENDENT CLAIMS are also included for (1) an antibody (A1); (2) reducing or inhibiting (M2) IL-22-induced and/or IL-20-induced proliferation or differentiation of hematopoietic cells and hematopoietic cell progenitors, involves culturing bone marrow or peripheral blood cells with a composition comprising (A1) or its fragment sufficient to reduce proliferation or differentiation of the hematopoietic cells in the bone marrow or peripheral blood cells as compared to bone marrow or peripheral blood cells cultured in the absence of (A1) or its fragment; (3) reducing IL-22-induced and/or IL-20-induced inflammation, involves administering to a mammal with inflammation, a composition of (A1) or its fragment sufficient to reduce inflammation; (4) suppressing an inflammatory response in a mammal with inflammation; (5) treating (M3) a mammal afflicted with an inflammatory disease in which IL-22 and/or IL-20 plays a role; (6) treating (M4) a mammal afflicted with an inflammatory disease in which IL-22RA plays a role, involves administering an antagonist of IL-22RA to the mammal such that the inflammation is reduced, where the antagonist comprises (A1) or its fragment, or binding polypeptide that specifically binds a polypeptide or polypeptide fragment of IL-22RA (SEQ ID Number 3), such that the inflammatory activity is reduced; and (7) reducing inflammation involves administering to a mammal with inflammation, a composition of (A1) to reduce inflammation.

WIDER DISCLOSURE - The following are disclosed: (1) fusion proteins comprising IL-22RA polypeptide and an immunoglobulin moiety; (2) isolated nucleic acid molecules encoding the fusion proteins; and (3) isolated IL-22RA polypeptide having a substantially similar sequence identity to the polypeptide of SEQ ID Number 3.

BIOTECHNOLOGY - Preferred Antibody: (A1) is chosen from: (a) an antibody produced by (M1), capable of binding to a polypeptide of SEQ ID Number 2 or 3, (b) an antibody or antibody fragment capable of binding to a polypeptide comprising a sequence of amino acid residues of SEQ ID Number 3, and capable of reducing the pro-inflammatory activity of either IL-20 (SEQ ID Number 8) or IL-22 (SEQ ID Number 6), and (c) an antibody comprising a monoclonal antibody that specifically binds to an antigenic epitope of human IL-22RA (SEQ ID Number 3) chosen from an epitope consisting of the amino acid sequence of SEQ ID Number 3 from amino acid number 1 (Pro)-amino acid number 6 (Asp), from amino acid number 26 (Ser)-amino acid number 32 (Pro), from amino acid number 41 (Lys)-amino acid number 47 (Asp), from amino acid number 41 (Lys)-amino acid number 62 (Cys), from amino acid number 84 (Ala)-amino acid number 97 (Ser), from amino acid number 103 (Thr)-amino acid number 108 (Asp), from amino acid number 130 (Arg)-amino acid number 135 (His), from amino acid number 164 (Gly)-amino acid number 166 (Lys), from amino acid number 175 (Tyr)-amino acid number 179 (Glu), from amino acid number 193 (Lys)-amino acid number 196 (Ala), or from amino acid number 203 (Lys)-amino acid number 209 (Thr), an epitope consisting of the amino acid sequence of SEQ ID Number 2 from amino acid number 49 (Val)-amino acid number 62 (Cys), and an epitope consisting of the amino acid sequence of SEQ ID Number 3 or 4, where the antibody reduces or neutralizes the activity of either human IL-22 (SEQ ID Number 6) or IL-20 (SEQ ID Number 8) Preferred Method: The antibody produced by (M1) reduces the pro-inflammatory activity of either/both IL-20 (SEQ ID Number 8) and/or IL-22 (SEQ ID Number 6). The antibody produced by (M1) neutralizes the interaction of either/both IL-20 (SEQ ID Number 8) and/or IL-22 (SEQ ID Number 6) with IL-22RA (SEQ ID Number 2). The neutralization by the antibody is measured by showing neutralization of either/both IL-20 (SEQ ID Number 8) and/or IL-22 (SEQ ID Number 6) in an in vitro cell-based neutralization assay. In (M2), the hematopoietic cells and hematopoietic progenitor cells are lymphoid cells, where the lymphoid cells are macrophages or T

cells. In (M3), (A1), its fragment or binding polypeptide further comprises radionuclide, enzyme, substrate, cofactor, fluorescent marker, chemiluminescent marker, peptide tag, magnetic particle, drug or toxin. In (M4), (A1), its fragment or binding polypeptide further comprises polyethylene glycol (PEG)ylation. Preferred Antibody: In (a) of (A1), the antibody is a polyclonal antibody, murine monoclonal antibody, humanized antibody derived from the murine monoclonal antibody, an antibody fragment, or a human monoclonal antibody.

(A1) further comprises a radionuclide, enzyme, substrate, cofactor, fluorescent marker, chemiluminescent marker, peptide tag, magnetic particle, drug or toxin, and PEGylation. In (b) of (A1), the antibody or its fragment reduces the pro-inflammatory activity of both IL-20 (SEQ ID Number 8) and IL-22 (SEQ ID Number 6). In (c) of (A1), the antibody reduces or neutralizes the activity of both human IL-22 (SEQ ID Number 6) and IL-20 (SEQ ID Number 8). (A1) is a murine monoclonal antibody, humanized antibody derived from the murine monoclonal antibody, an antibody fragment, or a human monoclonal antibody. Suppressing an inflammatory response in a mammal comprises: (a) determining a level of serum amyloid A protein, (b) administering a composition comprising (A1) or its fragment in a vehicle, (c) determining a post-administration level of serum amyloid A protein, and (d) comparing the level of serum amyloid A protein in step (a) to the level of serum amyloid A protein in step (c), where a lack of increase or decrease in serum amyloid A protein level is indicative of suppressing an inflammatory response. (M3) comprises administering an antagonist of IL-22 and/or IL-20 to the mammal such that the inflammation is reduced, where the antagonist comprises: (i) (A1) or its fragment, or binding polypeptide that specifically binds a polypeptide or polypeptide fragment of IL-22RA (SEQ ID Number 3), or (ii) a polypeptide or polypeptide fragment of IL-22RA (SEQ ID Number 3), where the inflammatory activity of either/both IL-22 (SEQ ID Number 6) and/or IL-20 (SEQ ID Number 8) is reduced.

ACTIVITY - Antiinflammatory; Gastrointestinal-Gen.; Antiulcer; Antiarthritic; Dermatological; Antipsoriatic; Antibacterial; Immunosuppressive; Antimicrobial; Antirheumatic; Antiarteriosclerotic; Antiasthmatic; Antidiabetic; Muscular-Gen.; Neuroprotective. In vivo analysis of the efficacy of antibodies raised against interleukin (IL)-22 receptor (IL-22RA) in treating psoriasis and colitis was carried out as follows. Severe combined immunodeficiency (SCID) mice were transferred with CD4+CD25- T cells to induce colitis. The mice were additionally injected with Staphylococcal enterotoxin B to develop psoriasis. The antibodies against IL-22RA were administered from days 0-21 after the cell transfer into the mice, and symptoms for colitis and psoriasis were monitored. Control group mice were administered with phosphate buffered saline. The result indicated inhibition of psoriatic and colitis symptoms in the antibody treated mice, compared to control group mice.

MECHANISM OF ACTION - IL-22RA inhibitor; Reduces IL-20 activity; Reduces IL-22 activity (all claimed).

USE - (M1) is useful for producing an antibody that specifically binds to an IL-22RA polypeptide. The treatment method is useful for treating a mammal afflicted with an inflammatory disease in which IL-22 and/or IL-20 plays a role, where the disease is a chronic inflammatory disease comprising inflammatory bowel disease, ulcerative colitis, Crohn's disease, arthritis, atopic dermatitis or psoriasis. The disease is an acute inflammatory disease comprising endotoxemia, septicemia, toxic shock syndrome or infectious disease. The method is useful for treating a mammal afflicted with an inflammatory disease in which IL-22RA plays a role, where the disease includes chronic inflammatory disease or acute inflammatory disease as mentioned above. The antibody is useful for treating a pathological condition in a subject associated with IL-22RA activity, which involves administering the antibody, thus treating the pathological condition. The pathological condition includes chronic inflammatory condition or acute inflammatory condition as mentioned above. The antibody is useful for reducing or inhibiting IL-22-induced

and/or IL-20-induced proliferation or differentiation of hematopoietic cells and hematopoietic cell progenitors, reducing IL-22-induced and/or IL-20-induced inflammation, suppressing an inflammatory response in a mammal with inflammation, treating a mammal afflicted with an inflammatory disease in which IL-22 and/or IL-20 plays a role or IL-22RA plays a role, and for reducing inflammation. (All claimed). The antibody is useful for diagnostic assays for determining circulating levels of soluble IL-22RA-comprising receptor polypeptides, and for treating rheumatoid arthritis, atherosclerosis, asthma, autoimmune diseases such as type I diabetes, multiple sclerosis, systemic lupus erythematosus, myasthenia gravis, etc.

ADMINISTRATION - The antibody is administered at a dosage of 0.1-100 (preferably 0.5-20) mg/kg body weight per day, by intravenous, intraarterial, intraperitoneal, intramuscular, subcutaneous, intrapleural, intrathecal or intralesional route.

EXAMPLE - No relevant example is given. (280 pages)

L4 ANSWER 2 OF 42 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2006-07772 BIOTECHDS
TI New polypeptide comprising a variant of a parent Fc region or its portion comprising an amino acid substitution at specific amino acid positions, for preparing a composition for treating e.g. cancer;
involving vector-mediated gene transfer and expression in Chinese hamster ovary, COS-1, yeast and Escherichia coli for cancer therapy
AU ALLAN B; JIANG W; TANG Y; WATKINS J D
PA APPLIED MOLECULAR EVOLUTION INC
PI WO 2006020114 23 Feb 2006
AI WO 2005-US25276 18 Jul 2005
PRAI US 2005-643718 13 Jan 2005; US 2004-598855 4 Aug 2004
DT Patent
LA English
OS WPI: 2006-174095 [18]
AN 2006-07772 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - A polypeptide comprising a variant of a parent Fc region or its portion comprising an amino acid substitution at one or more of amino acid positions 279, 341, 343 or 373 of the Fc region as compared to that in the parent Fc region, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a monoclonal antibody comprising the variant of a parent Fc region; (2) a process of producing a variant monoclonal antibody with enhanced antibody dependent cell-mediated cytotoxicity (ADCC) response as compared to the parent monoclonal antibody of the variant monoclonal antibody; (3) a process of producing a variant monoclonal antibody with diminished ADCC response as compared to the parent monoclonal antibody of the variant monoclonal antibody; (4) a process of producing a variant monoclonal antibody with enhanced FcRn binding affinity as compared to the parent monoclonal antibody of the variant monoclonal antibody; (5) a process of producing a variant monoclonal antibody with diminished FcRn binding affinity as compared to the parent monoclonal antibody of the variant monoclonal antibody; (6) a process of producing a variant monoclonal antibody with enhanced complement-dependent cytotoxicity (CDC) response as compared to the parent monoclonal antibody of the variant monoclonal antibody; (7) a process of producing a variant monoclonal antibody with diminished CDC response as compared to the parent monoclonal antibody of the variant monoclonal antibody; (8) a process of producing a variant polypeptide with enhanced serum half-life as compared to the parent polypeptide of the variant polypeptide; (9) a process of producing a variant polypeptide with diminished serum half-life as compared to the parent polypeptide of the variant polypeptide; (10) an isolated nucleic acid molecule comprising a nucleic acid molecule encoding a variant Fc region comprising at least one of the following amino acid substitutions in the Fc region: 235G, 235R, 236F, 236R, 236Y, 237K, 237N, 237R, 238E, 238G, 238H, 238I, 238L, 238V, 238W, 238Y, 244L,

245R, 247A, 247D, 247E, 247F, 247M, 247N, 247Q, 247R, 247S, 247T, 247W, 247Y, 248F, 248P, 248Q, 248W, 249L, 249M, 249N, 249P, 249Y, 251H, 251I, 251W, 254D, 254E, 254F, 254G, 254H, 254I, 254K, 254L, 254M, 254N, 254P, 254Q, 254R, 254V, 254W, 254Y, 255K, 255N, 256H, 256I, 256K, 256L, 256W, 256Y, 257A, 257I, 257M, 257N, 257S, 258D, 260S, 262L, 264S, 265K, 265S, 267H, 267I, 267K, 268K, 269N, 269Q, 271T, 272H, 272K, 272L, 272R, 279A, 279D, 279F, 279G, 279H, 279I, 279K, 279L, 279M, 279N, 279Q, 279R, 279S, 279T, 279W, 279Y, 280T, 283F, 283G, 283H, 283I, 283K, 283L, 283M, 283P, 283R, 283T, 283W, 283Y, 285N, 286F, 288N, 288P, 292E, 292F, 292G, 292I, 292L, 293S, 293V, 301W, 304E, 307E, 307M, 312P, 315F, 315K, 315L, 315P, 315R, 316F, 316K, 317P, 317T, 318N, 318P, 318T, 332F, 332G, 332L, 332M, 332S, 332V, 332W, 339D, 339E, 339F, 339G, 339H, 339I, 339K, 339L, 339M, 339N, 339Q, 339R, 339S, 339W, 339Y, 341D, 341E, 341F, 341H, 341I, 341K, 341L, 341M, 341N, 341P, 341Q, 341R, 341S, 341T, 341V, 341W, 341Y, 343A, 343D, 343E, 343F, 343G, 343H, 343I, 343K, 343L, 343M, 343N, 343Q, 343R, 343S, 343T, 343V, 343W, 343Y, 373D, 373E, 373F, 373G, 373H, 373I, 373K, 373L, 373M, 373N, 373Q, 373R, 373S, 373T, 373V, 373W, 375R, 376E, 376F, 376G, 376H, 376I, 376L, 376M, 376N, 376P, 376Q, 376R, 376S, 376T, 376V, 376W, 376Y, 377G, 377K, 377P, 378N, 379N, 379Q, 379S, 379T, 380D, 380N, 380S, 380T, 382D, 382F, 382H, 382I, 382K, 382L, 382M, 382N, 382P, 382Q, 382R, 382S, 382T, 382V, 382W, 382Y, 385E, 385P, 386K, 423N, 424H, 424M, 424V, 426D, 426L, 427N, 429A, 429F, 429M, 430A, 430D, 430F, 430G, 430H, 430I, 430K, 430L, 430M, 430N, 430P, 430Q, 430R, 430S, 430T, 430V, 430W, 430Y, 431H, 431K, 431P, 432R, 432S, 438G, 438K, 438L, 438T, 438W, 439E, 439H, 439Q, 440D, 440E, 440F, 440G, 440H, 440I, 440K, 440L, 440M, 440Q, 440T, 440V or 442K; (11) a vector comprising the isolated nucleic acid molecule; (12) a host cell comprising the vector; and (13) a pharmaceutical composition comprising the variant polypeptide or variant monoclonal antibody.

BIOTECHNOLOGY - Preferred Polypeptide: The polypeptide comprises a variant of a parent Fc region comprising at least one of the following amino acid substitutions of (10). The parent Fc region is a native Fc region. The parent Fc region is an IgG Fc region or its portion. The parent Fc region is an IgG1, IgG3 or IgG4 Fc region. The polypeptide is a monoclonal antibody. The monoclonal antibody is a chimeric, humanized or human monoclonal antibody. The monoclonal antibody is a full-length antibody or a single chain monoclonal antibody. The polypeptide comprises at least one of the following amino acid substitutions in the Fc region: 238L, 244L, 245R, 249P, 252Y, 256P, 257A, 257I, 257M, 257N, 257S, 257V, 258D, 260S, 262L, 270K, 272L, 272R, 279A, 279D, 279G, 279H, 279M, 279N, 279Q, 279R, 279S, 279T, 279W, 279Y, 283A, 283D, 283F, 283G, 283H, 283I, 283K, 283L, 283N, 283P, 283Q, 283R, 283S, 283T, 283W, 283Y, 285N, 286F, 288N, 288P, 293V, 307E, 307M, 311A, 311I, 311K, 311L, 311M, 311V, 311W, 312P, 316K, 317P, 318N, 318T, 332F, 332H, 332K, 332L, 332M, 332R, 332S, 332W, 339N, 339T, 339W, 341P, 343E, 343H, 343K, 343Q, 343R, 343T, 343Y, 375R, 376G, 376I, 376M, 376P, 376T, 376V, 377K, 378D, 378N, 380N, 380S, 380T, 382F, 382H, 382I, 382K, 382L, 382M, 382N, 382Q, 382R, 382S, 382T, 382V, 382W, 382Y, 423N, 427N, 430A, 430F, 430G, 430H, 430I, 430K, 430L, 430M, 430N, 430Q, 430R, 430S, 430T, 430V, 430Y, 431H, 431K, 434F, 434G, 434H, 434W, 434Y, 436I, 436L, 436T, 438K, 438L, 438T, 438W, 440K or 442K, where the polypeptide comprising the variant Fc region displays enhanced serum half-life as compared to the polypeptide comprising the parent Fc region. The polypeptide comprises at least one of the following amino acid substitutions in the Fc region: 245R, 252Y, 256P, 257A, 257I, 257M, 257N, 257S, 257V, 258D, 260S, 262L, 279A, 279D, 279G, 279H, 279N, 279Q, 279S, 279T, 279W, 279Y, 283F, 283H, 283K, 283R, 285N, 286F, 307E, 307M, 311I, 311K, 311L, 311M, 312P, 318N, 318T, 332S, 339W, 343E, 343H, 343K, 343Q, 343R, 375R, 377K, 378D, 378N, 380S, 380T, 382F, 382K, 382Q, 382R, 382S, 382T, 382V, 382W, 382Y, 423N, 427N, 430A, 430F, 430H, 430I, 430L, 430M, 430N, 430Q, 430R, 430S, 430V, 430Y, 431H, 431K, 434F, 434G, 434H, 434W, 434Y, 436I, 436L, 438K, 438L or 438W. The polypeptide comprises at least one of the following amino acid substitutions in the Fc region: 235Q, 236Y, 237K, 237R, 238E, 238G, 238H, 238W, 2471A, 247D, 247E, 247F, 247G, 247H, 247I, 247L, 247M, 247N, 247Q,

247R, 247S, 247W, 247Y, 248A, 248F, 248P, 248Q, 248W, 249E, 249L, 249M, 249Y, 251F, 251H, 251I, 251W, 254D, 254E, 254F, 254G, 254H, 254I, 254K, 254L, 254M, 254N, 254P, 254Q, 254R, 254T, 254V, 254W, 254Y, 255K, 255N, 256F, 256H, 256I, 256K, 256M, 246R, 256W, 256Y, 264S, 265S, 265Y, 267G, 267I, 268D, 268K, 270A, 270M, 279I, 279K, 279L, 280T, 292E, 292F, 292G, 292I, 292L, 311D, 311E, 311F, 311G, 311N, 311R, 311Y, 315F, 315K, 315P, 316F, 317T, 326W, 327T, 339E, 339G, 339L, 339R, 341D, 341E, 341F, 341I, 341K, 341L, 341M, 341N, 341Q, 341R, 341S, 341T, 341V, 341W, 341Y, 343M, 343V, 343W, 373A, 373D, 373G, 373K, 373L, 373M, 373N, 373Q, 373S, 373T, 373V, 373W, 376H, 376L, 376W, 376Y, 424M, 424V, 426D, 429A, 429F, 429M, 430D, 430W, 431P, 432R, 432S, 439Q, 440D, 440E, 440F or 440M, where the polypeptide comprising the variant Fc region displays diminished serum half-life as compared to the polypeptide comprising the parent Fc region. The polypeptide comprises at least one of the following amino acid

substitutions in the Fc region: 237R, 247D, 247E, 247F, 247H, 247L, 247M, 247N, 247Q, 247W, 247Y, 248A, 248F, 248P, 248Q, 248W, 249L, 249M, 249Y, 251H, 251I, 251W, 254D, 254E, 254F, 254G, 254H, 254I, 254K, 254M, 254N, 254P, 254Q, 254R, 254T, 254V, 254W, 254Y, 255K, 255N, 256F, 256H, 256K, 256M, 256R, 256W, 265Y, 280T, 292G, 292I, 311D, 311E, 311G, 311N, 315F, 315P, 316T, 317T, 327T, 341D, 341E, 341F, 341I, 341L, 341Y, 343W, 373A, 373G, 373M, 373Q, 376W, 376Y, 424M, 424V, 430D, 430W, 431P or 432S.

Preferred Antibody: The monoclonal antibody comprises at least one of the following amino acid substitutions in the Fc region: 247A, 247F, 247M, 247T, 247V, 247Y, 249E, 249Y, 254F, 254M, 254Y, 256A, 258D, 279A, 283A, 283I, 283K, 283M, 283R, 288N, 292A, 311A, 311D, 311N, 311T, 311V, 311Y, 315L, 318N, 318P, 318T, 318V, 332T, 332V, 339D, 339F, 339G, 339I, 339K, 339M, 339N, 339Q, 339R, 339S, 339T, 376A, 376V, 377G, 377K, 379N, 380N, 380S, 382A, 382I, 385E, 427N, 429M, 434W, 436I, 440G, 440H, 440I or 440L, where the monoclonal antibody comprising the variant of a parent Fc region displays enhanced ADCC as compared to the monoclonal antibody comprising the parent Fc region. The monoclonal antibody comprises at least one of the following amino acid substitutions in the Fc region:

235Q, 235R, 235S, 236F, 236R, 236Y, 237E, 237K, 237N, 237R, 238E, 238G, 238H, 238I, 238L, 238V, 238W, 238Y, 247G, 247R, 249L, 249P, 250K, 250M, 250R, 251H, 251I, 251W, 252Y, 254L, 254P, 254Q, 254T, 254V, 256V, 257A, 257I, 257M, 257N, 257S, 257V, 260S, 262L, 264S, 265H, 265K, 265S, 267G, 267H, 267I, 267K, 269N, 269Q, 270A, 270G, 270K, 270N, 271T, 272H, 272K, 272L, 272N, 272R, 279D, 279F, 279K, 279L, 279W, 283D, 283F, 283G, 283H, 283L, 283T, 283W, 283Y, 285N, 288P, 292E, 292F, 292G, 292I, 293S, 293V, 301W, 304E, 307A, 307E, 307M, 311F, 311I, 311K, 311S, 312P, 314F, 314I, 314V, 314W, 315F, 315P, 316F, 317P, 327T, 328V, 329Y, 332G, 332K, 332L, 332R, 332W, 341D, 341E, 341F, 341H, 341I, 341K, 341L, 341M, 341N, 341P, 341Q, 341R, 341S, 341T, 341W, 341Y, 343A, 343D, 343E, 343F, 343G, 343H, 343L, 343M, 343N, 343Q, 343R, 343S, 343T, 343V, 343W, 343Y, 373A, 373D, 373E, 373F, 373G, 373I, 373K, 373L, 373M, 373N, 373Q, 373R, 373S, 373T, 373V, 373W, 375R, 376A, 376E, 376F, 376G, 376H, 376W, 376Y, 379Q, 382D, 382S, 430H, 430K, 430N, 430Q, 430R, 430W, 432R, 432S, 434I, 440D, 440T, 440V or 442K, where the monoclonal antibody comprising the variant Fc region displays diminished ADCC as compared to the monoclonal antibody comprising the parent Fc region. The monoclonal antibody comprises at least one of the following amino acid substitutions in the Fc region:

235R, 236F, 236Y, 237E, 237K, 237N, 237R, 238E, 238G, 238H, 238I, 238L, 238V, 238W, 238Y, 247R, 250K, 251H, 254T, 257I, 257M, 257N, 257S, 257V, 265H, 265K, 265S, 267G, 267H, 267I, 267K, 269N, 269Q, 270A, 270G, 270K, 270M, 270N, 271T, 272N, 272R, 288P, 292E, 301W, 304E, 316F, 317P, 327T, 328V, 329Y, 332K, 332R, 341F, 341I, 341M, 341P, 341Q, 341R, 341T, 341W, 341Y, 343W, 373A, 373E, 373G, 373S, 376W, 432R or 432S. The monoclonal antibody comprises at least one of the following amino acid substitutions in the Fc region: 238L, 244L, 245R, 249P, 252Y, 256P, 257A, 257I, 257M, 257N, 257S, 258D, 260S, 262L, 270K, 272L, 272R, 279A, 279D, 279G, 279H, 279M, 279N, 279Q, 279R, 279S, 279T, 279W, 279Y, 283A, 283D, 283F, 283G, 283H, 283I, 283K, 283L, 283N, 283P, 283Q, 283R, 283S, 283T, 283W, 283Y, 285N, 286F, 288N, 288P, 293V, 307E, 307M, 311A, 311I, 311K, 311L, 311M, 311V, 311W, 312P, 316K, 317P, 318N, 318T, 332F, 332H, 332K, 332L, 332M,

332R, 332S, 332W, 339N, 339T, 339W, 341P, 343E, 343H, 343K, 343Q, 343R, 343T, 343Y, 375R, 376G, 376I, 376M, 376P, 376T, 376V, 377K, 378D, 378N, 380N, 380S, 380T, 382F, 382H, 382I, 382K, 382L, 382M, 382N, 382Q, 382R, 382S, 382T, 382V, 382W, 382Y, 423N, 427N, 430A, 430F, 430G, 430H, 430I, 430K, 430L, 430M, 430N, 430Q, 430R, 430S, 430T, 430V, 430Y, 431H, 431K, 434F, 434G, 434H, 434W, 434Y, 436I, 436L, 436T, 438K, 438L, 438T, 438W, 440K or 442K, where the monoclonal antibody comprising the variant Fc region displays enhanced FcRn binding affinity as compared to the monoclonal antibody comprising the parent Fc region. The monoclonal antibody comprises at least one of the following amino acid substitutions in the Fc region: 245R, 252Y, 256P, 257A, 257I, 257M, 257N, 257S, 257V, 258D, 260S, 262L, 279A, 279D, 279G, 279H, 279N, 279Q, 279S, 279T, 279W, 279Y, 283F, 283H, 283K, 283R, 285N, 286F, 307E, 307M, 311I, 311K, 311M, 312P, 318N, 318T, 332S, 339W, 343E, 343H, 343K, 343Q, 343R, 375R, 377K, 378D, 378N, 380S, 380T, 382F, 382K, 382Q, 382R, 382S, 382T, 382V, 382W, 382Y, 423N, 427N, 430A, 430F, 430H, 430I, 430L, 430M, 430N, 430Q, 430R, 430S, 430V, 430Y, 431H, 431K, 434F, 434G, 434H, 434I (sic), 434Y, 436I, 436L, 438K, 438L or 438W. The monoclonal antibody comprises at least one of the following amino acid substitutions in the Fc region: 235Q, 236Y, 237K, 237R, 238E, 238G, 238H, 238W, 247A, 247D, 247E, 247F, 247G, 247H, 247I, 247L, 247M, 247N, 247Q, 247R, 247S, 247W, 247Y, 248A, 248F, 248P, 248Q, 248W, 249E, 249L, 249M, 249Y, 251F, 251H, 251I, 251W, 254D, 254E, 254F, 254G, 254H, 254I, 254K, 254L, 254M, 254N, 254P, 254Q, 254R, 254T, 254V, 254W, 254Y, 255K, 255N, 256F, 256H, 256I, 256K, 256M, 256R, 256W, 256Y, 264S, 265S, 265Y, 267G, 267I, 268D, 268K, 270A, 270M, 279I, 279K, 279L, 280T, 292E, 292F, 292G, 292I, 292L, 311D, 311E, 311F, 311G, 311N, 311R, 311Y, 315F, 315K, 315P, 316F, 317T, 326W, 327T, 339E, 339G, 339L, 339R, 341D, 341E, 341F, 341I, 341K, 341L, 341M, 341N, 341Q, 341R, 341S, 341T, 341V, 341W, 341Y, 343M, 343V, 343W, 373D, 373G, 373A, 373D, 373G, 373K, 373L, 373M, 373N, 373Q, 373S, 373T, 373V, 373W, 376H, 376L, 376W, 376Y, 424M, 424V, 426D, 429A, 429F, 429M, 430D, 430W, 431P, 432R, 432S, 439Q, 440A, 440D, 440E, 440F or 440M, where the monoclonal antibody comprising the variant Fc region displays diminished FcRn binding affinity as compared to the monoclonal antibody comprising the parent Fc region. The monoclonal antibody comprises at least one of the following amino acid substitutions in the Fc region: 237R, 247D, 247E, 247F, 247H, 247I, 247L, 247M, 247N, 247Q, 247W, 247Y, 248A, 248F, 248P, 248Q, 248W, 249L, 249M, 249Y, 251H, 251I, 251W, 254D, 254E, 254F, 254G, 254H, 254I, 254K, 254M, 254N, 254P, 254Q, 254R, 254T, 254V, 254W, 254Y, 255K, 255N, 256F, 256H, 256K, 256M, 256R, 256W, 265Y, 280T, 292G, 292I, 311D, 311E, 311G, 311N, 315F, 315P, 316T, 317T, 327T, 341D, 341E, 341F, 341I, 341L, 341Y, 343W, 373A, 373G, 373M, 373Q, 376W, 376Y, 424M, 424V, 430D, 430W, 431P or 432S. The monoclonal antibody comprises at least one of the following amino acid substitutions in the Fc region: 236Y, 244L, 247A, 247D, 247E, 247G, 247N, 247Q, 247R, 247S, 247W, 248F, 248P, 248Q, 248W, 249E, 249L, 249M, 249N, 249P, 249Y, 251F, 251H, 251I, 251W, 254A, 254F, 254K, 254L, 254M, 254R, 254Y, 255K, 256A, 256G, 256I, 256L, 256M, 256P, 256Q, 256W, 256Y, 260S, 268D, 279Q, 279S, 279W, 279Y, 280K, 280T, 283F, 283G, 283H, 283I, 283K, 283L, 283M, 283N, 283P, 283R, 283S, 283W, 292L, 307A, 307M, 311F, 311I, 311K, 311L, 311M, 311T, 311V, 311W, 311Y, 312P, 314F, 314I, 314V, 314W, 314Y, 315F, 315K, 315L, 315P, 315R, 316K, 317P, 317T, 318N, 318T, 332A, 332D, 332E, 332F, 332G, 332L, 332M, 332Q, 332S, 332T, 332V, 332W, 332Y, 339D, 339F, 339G, 339H, 339I, 339K, 339N, 339Q, 339R, 339S, 339T, 339W, 339Y, 341D, 341E, 341F, 341H, 341I, 341K, 341L, 341M, 341N, 341P, 341Q, 341R, 341S, 341T, 341V, 341W, 341Y, 343A, 343D, 343E, 343G, 343H, 343K, 343L, 343M, 343N, 343Q, 343R, 343S, 343T, 343W, 343Y, 373D, 373E, 373F, 373H, 373I, 373K, 373L, 373M, 373N, 373Q, 373R, 373T, 373V, 373W, 375R, 376A, 376F, 376G, 376H, 376L, 376N, 376P, 376Q, 376R, 376S, 376T, 376V, 377P, 379N, 379Q, 379S, 379T, 380A, 380N, 380S, 380T, 382I, 382L, 382Q, 382V, 386K, 426D, 426L, 429A, 429F, 429M, 430A, 430D, 430F, 430G, 430H, 430I, 430K, 430L, 430M, 430N, 430P, 430R, 430S, 430T, 430V, 430W, 430Y, 431H, 431P, 432R, 432S, 438L, 438W, 434Y, 438L, 438W, 440Q or 440Y, where the monoclonal antibody comprising the variant Fc region displays enhanced CDC activity as compared to the monoclonal

antibody comprising the parent Fc region. The monoclonal antibody comprises at least one of the following amino acid substitutions in the Fc region: 235G, 236R, 235S, 237K, 237E, 237K, 237N, 237R, 238A, 238E, 238G, 238H, 238I, 238L, 238V, 238W, 238Y, 245R, 247H, 247I, 247L, 247T, 247Y, 250M, 252Y, 254D, 254E, 254I, 254P, 254Q, 254T, 254V, 255N, 257A, 257I, 257M, 257N, 257S, 257V, 262L, 264S, 265H, 265Y, 267G, 267H, 267I, 267K, 268K, 269N, 269Q, 270G, 270M, 270N, 271T, 272H, 272L, 272N, 292A, 293S, 301W, 307E, 311E, 311S, 316F, 318P, 327T, 328V, 329Y, 330K, 330R, 332E, 332M, 343I, 373S, 378D, 380D, 382D, 382F, 382N, 382P, 382R, 382S, 382W, 382Y, 385E, 385P, 423N, 424H, 424M or 427N, where the monoclonal antibody comprising the variant Fc region displays diminished CDC activity as compared to the monoclonal antibody comprising the parent Fc region. The monoclonal antibody is a chimeric, humanized or human monoclonal antibody. The monoclonal antibody is a full-length antibody or a single chain monoclonal antibody. The antibody specifically binds a human target antigen consisting of CD3, CD20, CD25, TNFalpha, Her2/neu, CD33, CD52, epidermal growth factor receptor (EGFR), EpCAM, MUC1, GD3, carcinoembryonic antigen (CEA), CA125, HLA-DR, transforming growth factor (TGF)beta, vascular endothelial growth factor (VEGF), GDF8, GDF11, ghrelin, or its any precursor or functional fragment. The antibody is an anti-CD20 antibody comprising: (1) a light chain variable region amino acid sequence consisting of SEQ ID NO: 13; (2) a heavy chain variable region amino acid sequence consisting of a 213 amino acid sequence (SEQ ID NO: 14); or (3) a variant of a parent Fc region where the variant Fc region comprises an amino acid substitution consisting of 247I/339Q, 247F339D or 378D. The anti-CD20 antibody comprises a light chain amino acid sequence consisting of SEQ ID NO: 29 and a heavy chain consisting of a 451 amino acid sequence (SEQ ID NO: 31, 33 or 35). The sequences are given in the specification. Preferred Vector: The vector is an expression vector. Preferred Host Cell: The host cell type is Chinese Hamster Ovary (CHO), COS, SP2/0, NSO, yeast, Escherichia coli or its derivative or progeny. Preferred Composition: The pharmaceutical composition comprises the anti-CD20 antibody. Preferred Method: Producing the variant monoclonal antibodies comprises engineering the Fc region of the parent monoclonal antibody to comprise at least one of the amino acid substitutions. Producing the variant polypeptide comprises: (1) expressing the variant polypeptide from a nucleic acid molecule encoding the parent polypeptide operably linked to a nucleic acid molecule encoding a Fc region comprising at least one of the amino acid substitutions; and (2) isolating and purifying the variant polypeptide.

ACTIVITY - Cytostatic. No biological data given.

MECHANISM OF ACTION - CD20 antagonist.

USE - The polypeptide is useful in preparing a composition for treating e.g., cancer.

ADMINISTRATION - Dosage comprises 1-100 mg/kg body weight. The composition is administered via oral or parenteral route.

EXAMPLE - No relevant examples given. (193 pages)

L4 ANSWER 3 OF 42 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2005-30525 BIOTECHDS
TI New human monoclonal antibody that
specifically binds to human CD20, useful for treating or preventing a
disease or disorder involving cells expressing CD20, e.g. lymphoma,
leukemia and autoimmune diseases;
involving vector-mediated gene transfer and expression in host cell
for gene therapy
AU TEELING J; GLENNIE M; PARREN P; GERRITSEN A F; RUULS S; GRAUS Y; VAN DE
WINKEL J
PA GENMAB AS
PI WO 2005103081 3 Nov 2005
AI WO 2005-DK270 20 Apr 2005
PRAI DK 2004-627 20 Apr 2004; DK 2004-627 20 Apr 2004
DT Patent

LA English
OS WPI: 2005-734711 [75]
AN 2005-30525 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - A human monoclonal antibody that specifically binds to human CD20, and which comprises a heavy chain variable region and a light chain variable region, where the heavy chain variable region contains the VH CDR3 of 14 amino acids (SEQ ID Number 10), given in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a hybridoma which produces a human monoclonal antibody against CD20 encoded by human heavy chain and human light chain nucleic acids; (2) a transfectoma which produces a human monoclonal antibody against CD20; (3) a eukaryotic or prokaryotic host cell which produces the human monoclonal antibody, or its conservative sequence modifications; (4) a pharmaceutical composition comprising the human monoclonal antibody, and a carrier; (5) an immunoconjugate comprising an antibody linked to a cytotoxic agent, a radioisotope, or a drug; (6) a bispecific molecule comprising an antibody, and a binding specificity for a human effector cell, or a human Fc receptor or a binding specificity for a T cell receptor, such as CD3; (7) treating or preventing a disease or disorder involving cells expressing CD20, comprising administering to a subject the human monoclonal antibody, pharmaceutical composition, immunoconjugate, or bispecific molecule, or an expression vector in an amount effective to treat or prevent the disease or disorder; (8) an in vitro method for detecting the presence of CD20 antigen, or a cell expressing CD20, in a sample comprising: contacting the sample with the antibody under conditions that allow for formation of a complex between the antibody and CD20; and detecting the formation of a complex; (9) a kit for detecting the presence of CD20 antigen, or a cell expressing CD20, in a sample comprising the antibody; (10) an in vivo method for detecting CD20 antigen, or a cell expressing CD20, in a subject comprising: administering the antibody under conditions that allow for formation of a complex between the antibody and CD20; and detecting the formed complex; (11) an expression vector comprising the nucleotide sequence of the heavy chain or light chain region; (12) a pharmaceutical composition comprising the expression vector, and a carrier; and (13) an anti-idiotypic antibody binding to the antibody, or to 2C6 IgG1, K.

BIOTECHNOLOGY - Preferred Antibody: The human monoclonal antibody comprises the VH CDR1, VH CDR2 and VH CDR3. The antibody comprises the VH region of 123 amino acids (SEQ ID Number 2), or a VH region, which is at least 90, 95, 98 or 99% homologous to SEQ ID Number 2. The antibody comprises VL CDR1, VL CDR2, and VL CDR3. The antibody comprises the VL region of 106 amino acids (SEQ ID Number 5) or 107 amino acids (SEQ ID Number 4), or a VL region, which is at least 90, 95, 98 or 99% homologous to SEQ ID Number 5. The antibody is an IgG1 or IgM antibody, preferably and IgG1,kappa or IgM,kappa antibody. The antibody is encoded by human heavy chain nucleic acids and human kappa light chain nucleic acids comprising variable heavy chain nucleotide sequence 369 base pairs (SEQ ID Number 1), and variable light chain nucleotide sequence of 321 bp (SEQ ID Number 3 or 6), or their conservative sequence modifications. The antibody is an antibody fragment or a single chain antibody. The antibody is a binding-domain immunoglobulin fusion protein comprising: a binding domain polypeptide in the form of a heavy chain variable region or a light chain variable region that is fused to an immunoglobulin hinge region polypeptide; an immunoglobulin heavy chain CH2 constant region fused to the hinge region; and an immunoglobulin heavy chain CH3 constant region fused to the CH2 constant region. The human CD20 comprises a heavy chain variable region derived from human germline sequence VH3-20 and a light chain variable region derived from human germline sequence VkappaIII-L6 or VkappaI-L15. The antibody does not bind to CD20 mutants mutated at positions 163 or 166. The antibody

binds to a discontinuous epitope on CD20, where the epitope has part of the first small extracellular loop and part of the second extracellular loop. The antibody further comprises a chelator linker for attaching a radioisotope. Preferred Composition: The pharmaceutical composition comprises one or more further therapeutic agents. Preferred Method: Treating or preventing a disease or disorder comprises administering one or more further therapeutic agents to the subject. The therapeutic agents are selected from chemotherapeutic agents, anti-inflammatory drugs, disease modifying anti-rheumatic drugs (DMARDs), and immunosuppressive agents. Therapeutic agents are selected from antimetabolites (e.g., methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, fludarabine, 5-fluorouracil, decarbazine, hydroxyurea, azathioprin, gemcitabine and cladribine), alkylating agents (e.g., mechlorethamine, thioepa, chlorambucil, melphalan, carmustine (BSNU) and lomustine (CCNU), cyclophosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cis-dichlorodiamine platinum (II) (DDP) cisplatin), anthracyclines (e.g., daunorubicin (formerly daunomycin) and doxorubicin), antibiotics (e.g., dactinomycin (formerly actinomycin), bleomycin, mithramycin, and anthramycin (AMC)), and anti-mitotic agents (e.g., vincristine, vinblastine, docetaxel, paclitaxel and vinorelbin). The therapeutic agent is selected from doxorubicin, cisplatin, bleomycin, carmustine, chlorambucil, and cyclophosphamide. The therapeutic agent is an immunological modulating agent, such as a cytokine or a chemokine. The therapeutic agent is selected from anti-CD25 antibodies, anti-CD19 antibodies, anti-CD21 antibodies, anti-CD22 antibodies, anti-CD37 antibodies, anti-CD38 antibodies, anti-IL6R antibodies, anti-IL8 antibodies, anti-IL15 antibodies, anti-IL15R antibodies, anti-CD4 antibodies, anti-CD11a antibodies, anti-alpha-4/beta-1 integrin (VLA4) antibodies, CTLA4-Ig, and anti- C3b(i) antibodies. Preferred Vector: The expression vector further comprises a nucleotide sequence encoding the constant region of a light chain, heavy chain or both light and heavy chains of a human antibody, which binds to human CD20.

ACTIVITY - Cytostatic; Immunosuppressive; Virucide; Nephrotropic; Antiinflammatory; Dermatological; Metabolic-Gen; Respiratory-Gen. No biological data given.

MECHANISM OF ACTION - Antibody therapy; Gene Therapy.

USE - The antibody, compositions, molecules, immunoconjugate, vector and methods are useful for treating or preventing a disease or disorder involving cells expressing CD20, e.g. B cell lymphoma, B cell non-Hodgkin's lymphoma (NHL), precursor B cell lymphoblastic leukemia/lymphoma and mature B cell neoplasms, such as B cell chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL), B cell prolymphocytic leukemia, lymphoplasmacytic lymphoma, mantle cell lymphoma (MCL), follicular lymphoma (FL), cutaneous follicle center lymphoma, marginal zone B cell lymphoma (MALT type, nodal and splenic type), hairy cell leukemia, diffuse large B cell lymphoma, Burkitt's lymphoma, plasmacytoma, plasma cell myeloma, post-transplant lymphoproliferative disorder, Waldenstrom's macroglobulinemia, anaplastic large-cell lymphoma (ALCL), lymphomatoid granulomatosis, primary effusion lymphoma, intravascular large B cell lymphoma, mediastinal large B cell lymphoma, heavy chain diseases (including γ , μ , and α disease), lymphomas induced by therapy with immunosuppressive agents, such as cyclosporine-induced lymphoma, and methotrexate-induced lymphoma. The disease or disorder is follicular lymphoma (FL). They are particularly useful for treating psoriasis, psoriatic arthritis, dermatitis, systemic sclerosis, inflammatory bowel disease (IBD), Crohn's disease, ulcerative colitis, respiratory distress syndrome, meningitis, encephalitis, uveitis, glomerulonephritis, eczema, asthma, atherosclerosis, leukocyte adhesion deficiency, multiple sclerosis, Raynaud's syndrome, Sjogren's syndrome, juvenile onset diabetes, Reiter's disease, Behcet's disease, immune complex nephritis, IgA nephropathy, IgM polyneuropathies, immune-mediated thrombocytopenias, such as acute idiopathic thrombocytopenic purpura and chronic idiopathic thrombocytopenic purpura, hemolytic anemia, myasthenia gravis, lupus nephritis, systemic lupus erythematosus, rheumatoid

arthritis (RA), atopic dermatitis, pemphigus (including pemphigus vulgaris), Graves' disease, Hashimoto's thyroiditis, Wegener's granulomatosis, Omenn's syndrome, chronic renal failure, acute infectious mononucleosis, HIV, herpes virus associated diseases, and as well as diseases and disorders caused by or mediated by infection of B-cells with virus, such as Epstein-Barr virus (EBV). The anti-idiotypic antibody is useful for detecting the level of human monoclonal antibody against CD20 in a sample. (All claimed).

ADMINISTRATION - Dosage is 50-4000 mg per week. Administration is oral, nasal, topical (buccal or sublingual), rectal, vaginal, and/or parenteral.

EXAMPLE - No relevant examples given. (106 pages)

L4 ANSWER 4 OF 42 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN

AN 2005-14048 BIOTECHDS

TI New antibody that binds a CXCR3 protein and comprising heavy and light chain complementarity determining regions, useful in preparing a composition for treating inflammatory disorder;
involving vector-mediated gene transfer and expression in hybridoma cell culture

AU QIN S; KASSAM N; NEWMAN W

PA MILLENNIUM PHARM INC

PI WO 2005030793 7 Apr 2005

AI WO 2004-US31445 24 Sep 2004

PRAI US 2003-505697 24 Sep 2003; US 2003-505697 24 Sep 2003

DT Patent

LA English

OS WPI: 2005-262947 [27]

AN 2005-14048 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - A new antibody or its antigen-binding fragment binds a CXCR3 protein and comprises heavy and light chain complementarity-determining regions.

DETAILED DESCRIPTION - A new antibody or its antigen-binding fragment binds a CXCR3 protein and comprises: (1) at least one heavy chain complementarity determining region consisting of HCDR1, HCDR2 or HCDR3 comprising a sequence having 5, 17 or 17 amino acids (SEQ ID NO: 4 or 20 or SEQ ID NO: 4 or 20 where one amino acid residue is conservatively substituted; SEQ ID NO: 6 or 22 or SEQ ID NO: 6 or 22 where one or two amino acid residues are conservatively substituted; or SEQ ID NO: 8 or 24 or SEQ ID NO: 8 or 24 where one, two or three amino acid residues are conservatively substituted); and (2) at least one light chain complementarity determining region consisting of LCDR1, LCDR2 or LCDR3 comprising a sequence having 11, 7 or 9 amino acids (SEQ ID NO: 12 or 28 or SEQ ID NO: 12 or 28 where one or two amino acid residues are conservatively substituted; SEQ ID NO: 14 or 30 or SEQ ID NO: 14 or 30 where one amino acid residue is conservatively substituted; or SEQ ID NO: 16 or 32 or SEQ ID NO: 16 or 32 where one or two amino acids are conservatively substituted). INDEPENDENT CLAIMS are also included for: (1) an isolated cell which produces the antibody or antigen-binding fragment; (2) a hybridoma consisting of hybridoma 5H7 (ATCC Accession Number PTA-5388) or hybridoma 7H5 (ATCC Accession Number PTA-5389); (3) an immunoglobulin heavy or light chain or its antigen-binding portion of the antibody produced by hybridoma 5H7 (ATCC Accession Number PTA-5388) or hybridoma 7H5 (ATCC Accession Number PTA-5389) and comprising three heavy or light chain complementarity determining regions; (4) an isolated and/or recombinant nucleic acid comprising a nucleotide sequence that encodes the immunoglobulin heavy or light chain or antigen-binding portion; (5) an expression construct comprising the recombinant nucleic acid that encodes the immunoglobulin heavy or light chain; (6) a host cell comprising the recombinant nucleic acid that encodes the immunoglobulin heavy or light chain or antigen-binding portion; (7) an isolated cell that produces the immunoglobulin heavy or light chain or antigen-binding portion; (8) a composition comprising the antibody or antigen-binding

fragment and a carrier; and (9) treating a subject having an inflammatory disorder.

BIOTECHNOLOGY - Preferred Antibody: The antibody or its antigen-binding fragment binds a CXCR3 protein and comprises: (1) at least one heavy chain complementarity determining region consisting of HCDR1, HCDR2 or HCDR3 comprising a sequence having 5, 17 or 17 amino acids (SEQ ID NO: 4 or 20 or SEQ ID NO: 4 or 20 where one amino acid residue is conservatively substituted; SEQ ID NO: 6 or 22 or SEQ ID NO: 6 or 22 where one or two amino acid residues are conservatively substituted; or SEQ ID NO: 8 or 24 or SEQ ID NO: 8 or 24 where one, two or three amino acid residues are conservatively substituted); and (2) at least one light chain complementarity determining region consisting of LCDR1, LCDR2 or LCDR3 comprising a sequence having 11, 7 or 9 amino acids (SEQ ID NO. 12 or 28 or SEQ ID NO: 12 or 28 where one or two amino acid residues are conservatively substituted; SEQ ID NO: 14 or 30 or SEQ ID NO: 14 or 30 where one amino acid residue is conservatively substituted; or SEQ ID NO: 16 or 32 or SEQ ID NO: 16 or 32 where one or two amino acids are conservatively substituted). The antibody or its antigen-binding fragment inhibits binding of a ligand to the CXCR3 protein; inhibits a function of a CXCR3 protein consisting of CXCR3 ligand-induced intracellular calcium release, CXCR3 ligand-induced chemotaxis, CXCR3 ligand-induced cell differentiation, CXCR3 ligand-induced cell proliferation and CXCR3 ligand-induced cell activation; competitively inhibits binding of human monoclonal antibody 5H7 or human monoclonal antibody 7H5 to the CXCR3 protein; or has the epitopic specificity of human monoclonal antibody 5H7 or human monoclonal antibody 7H5. The CXCR3 ligand is IP-10, MIG or I-TAC. The antibody is a human antibody, an antigen-binding fragment of a human antibody, a humanized antibody, an antigen-binding fragment of a humanized antibody, a chimeric antibody or an antigen-binding fragment of a chimeric antibody. The antigen-binding fragment is an antigen-binding fragment consisting of Fab fragment, Fab' fragment, an F(ab')₂ fragment or an Fv fragment. The heavy chain variable region is encoded by a sequence having 378 (SEQ ID NO. 1 or 17) and comprises 126 amino acids and the light chain variable region is encoded by 321 (SEQ ID NO. 9 or 25) and comprises 107 amino acids. The antibody comprises the antibody produced by hybridoma 5H7 (ATCC Accession Number PTA-5388) or the antibody produced by hybridoma 7H5 (ATCC Accession Number PTA-5389) or its antigen-binding fragment. The immunoglobulin light or heavy chain or antigen-binding portion comprises a human immunoglobulin light or heavy chain, a humanized immunoglobulin light or heavy chain or a chimeric immunoglobulin light or heavy chain or antigen-binding portion. Preferred Method: Treating a subject having an inflammatory disorder comprises administering to the subject the antibody or antigen-binding fragment.

ACTIVITY - Antiinflammatory. No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The antibody or its antigen-binding fragment is useful in preparing a composition for treating inflammatory disorder (claimed).

ADMINISTRATION - Dosage comprises 0.01-20 mg/kg body weight. The composition is administered via oral or parenteral route.

EXAMPLE - No relevant examples given. (78 pages)

L4 ANSWER 5 OF 42 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2005-14670 BIOTECHDS
TI Treating respiratory disease e.g. asthma or Th2-cell mediated allergic disease in patient in need of such treatment, involves administering pharmaceutical formulation comprising antibody that specifically binds to IL-2 receptor;
method of respiratory and allergic disease therapy involving the use of a pharmaceutical composition comprising a humanized antibody specific for the interleukin-2 receptor
AU SHAMES R S

PA PROTEIN DESIGN LABS INC
PI WO 2005030252 7 Apr 2005
AI WO 2004-US31640 21 Sep 2004
PRAI US 2004-552974 12 Mar 2004; US 2003-505883 23 Sep 2003
DT Patent
LA English
OS WPI: 2005-285106 [29]
AN 2005-14670 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - Treating (M1) a respiratory disease or Th2-cell mediated allergic disease in patient in need of such treatment, involves administering to patient a therapeutically effective amount of pharmaceutical formulation comprising antibody that binds specifically to an IL-2 receptor.

BIOTECHNOLOGY - Preferred Method: In (M1), the antibody is humanized antibody. The humanized antibody is daclizumab. The antibody binds to the sample epitope as daclizumab. The antibody has an amino acid sequence that is at least 80% identical to the amino acid sequence of daclizumab. The pharmaceutical formulation is liquid comprising about 100 mg/ml daclizumab, 20-260 mM succinate buffer having pH from about 5.5-6.5, 0.01-0.1% polysorbate, and a tonicity buffer that contributes to isotonicity. (M1) preferably involves treating asthma (chronic, persistent asthma or moderate to severe asthma), where the method further involves administering to the patient one or more agents chosen from beclomethasone, budesonide, flunisolide, fluticasone, triamcinolone, memetasone and acetone, and the antibody has binding affinity for the human interleukin (IL)-2 receptor of at least 10⁸ M⁻¹, preferably 10⁹ M⁻¹. The antibody is a monoclonal, chimeric, human or humanized antibody. The antibody has complementarity determining regions (CDR) that have amino acid sequences that are at least 95% identical to the amino acid sequences of the CDR regions of daclizumab.

ACTIVITY - Antiasthmatic; Antiallergic; Antiinflammatory; Dermatological; Respiratory-Gen.

MECHANISM OF ACTION - IL-2 receptor specific antibody therapy (claimed). No supporting data is given.

USE - (M1) is useful for treating a respiratory disease or Th2-cell mediated allergic disease in patient in need of such treatment. The respiratory disease is chosen from asthma, allergic rhinitis, atopic dermatitis, nasal polyposis, Churg-Strauss syndrome, sinusitis, and chronic obstructive pulmonary disease (COPD), and the Th2-cell mediated allergic disease is chosen from any one of the above diseases except COPD (claimed).

ADMINISTRATION - In (M1), the pharmaceutical formulation is administered parenterally, intravenously, intramuscularly, or subcutaneously, at a therapeutically effective amount of between about 0.001-10 mg/kg, preferably between 0.5 and 4.0 mg/kg, or as a fixed dose of between about 100 mg and 200 mg (claimed). (62 pages)

L4 ANSWER 6 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1

AN 2004:452955 CAPLUS

DN 141:22207

TI Human monoclonal antibodies against CD25

IN Schuurman, Janine; Havenith, Catharina Emanuele Gerarda; Parren, Paul; Van De Winkel, Jan G. J.; Williams, Denise Leah; Petersen, Jorgen; Baadsgaard, Ole

PA Genmab A/s, Den.

SO PCT Int. Appl., 114 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.

KIND

DATE

APPLICATION NO.

DATE

PI	WO 2004045512	A2	20040603	WO 2003-US36126	20031114
	WO 2004045512	A3	20051124		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2505991	AA	20040603	CA 2003-2505991	20031114
	AU 2003295471	A1	20040615	AU 2003-295471	20031114
	US 2004170626	A1	20040902	US 2003-714353	20031114
	EP 1578397	A2	20050928	EP 2003-786661	20031114
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003016282	A	20051011	BR 2003-16282	20031114
	NO 2005002889	A	20050718	NO 2005-2889	20050614
PRAI	US 2002-426690P	P	20021115		
	WO 2003-US36126	W	20031114		

AB Isolated human monoclonal antibodies which bind to and inhibit human CD25, and related antibody-based compns. and mols., are disclosed. The human antibodies can be produced by a hybridoma, a transfectoma or in a nonhuman transgenic animal, e.g., a transgenic mouse, capable of producing multiple isotypes of human monoclonal antibodies by undergoing V(D)J recombination and isotype switching. Also disclosed are pharmaceutical compns. comprising the human antibodies, nonhuman transgenic animals, hybridomas and transfectomas which produce the human antibodies, and therapeutic and diagnostic methods for using the human antibodies.

L4 ANSWER 7 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:944197 CAPLUS

DN 142:446000

TI Recombinant anti-CD25 monoclonal antibodies for preventing and treating transplantation rejection

IN Ma, Jing

PA Peop. Rep. China

SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 21 pp.

CODEN: CNXXEV

DT Patent

LA Chinese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CN 1467223	A	20040114	CN 2002-112493	20020712
PRAI	CN 2002-112493		20020712		

AB The invention provides the amino acid sequences and DNA sequences of human anti-CD25 monoclonal antibody, VH and VL, and complementarity determining regions (CDRs). Antibodies comprising the CDRs are useful for preventing and treating transplant rejection.

L4 ANSWER 8 OF 42 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN

AN 2004-14322 BIOTECHDS

TI New human monoclonal antibodies against CD20, useful for diagnosing, preventing or treating diseases involving cells expressing CD20, e.g. cancer, psoriasis, HIV, glomerulonephritis, asthma, atherosclerosis or anemia;

monoclonal antibody with a cytotoxic agent, radioisotope or drug attached forming a therapeutic immunoconjugate for disease therapy

AU TEELING J; RUULS S; GLENNIE M; VAN DE WINKEL J G J; PARREN P; PETERSEN J;

PA BAADSGAARD O D M S; HUANG H
PI GENMAB AS; MEDAREX INC
WO 2004035607 29 Apr 2004
AI WO 2003-US33057 17 Oct 2003
PRAI US 2003-460028 2 Apr 2003; US 2002-419163 17 Oct 2002
DT Patent
LA English
OS WPI: 2004-348434 [32]
AN 2004-14322 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - An isolated human monoclonal antibody which binds to human CD20, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a hybridoma comprising a B cell obtained from a transgenic non-human animal in which V-(D)-J gene segment rearrangements have resulted in the formation of a functional human heavy chain transgene and a functional light chain transgene fused to an immortalized cell, where the hybridoma produces a detectable amount of the monoclonal antibody cited above; (2) a transfectoma comprising nucleic acids encoding a human heavy chain and a human light chain, where the transfectoma produces a detectable amount of the antibody cited above; (3) a eukaryotic or prokaryotic host cell which produces the human monoclonal antibody having heavy chain and light chain variable regions which comprise any of the 3 sequences of 141 or 144 amino acids and any of the 3 sequences having 127 amino acids each fully defined in the specification, respectively, and conservative sequence modifications; (4) a transgenic non-human animal or plant which produces the above human monoclonal antibody; (5) producing a human monoclonal antibody which binds to human CD20; (6) a pharmaceutical composition comprising the human antibody or a vector, and a pharmaceutical carrier, or a combination of two or more human antibodies having complementary functional activities; (7) an immunoconjugate comprising the above antibody linked to a cytotoxic agent, a radioisotope or a drug; (8) a bispecific molecule comprising the antibody and a binding specificity for a human effector cell or for a human Fc receptor or a binding specificity for a T cell receptor, such as CD3; (9) inhibiting growth of a cell expressing CD20; (10) killing a cell expressing CD20; (11) treating or preventing a disease or disorder involving cells expressing CD20; (12) an in vitro or in vivo method for detecting the presence of CD20 antigen, or a cell expressing CD20, in a sample or a subject; (13) a kit for detecting the presence of CD20 antigen, or a cell expressing CD20, in a sample comprising the antibody; (14) an expression vector comprising a nucleotide sequence encoding the variable region of a light chain, heavy chain or both light and heavy chains of the above human antibody which binds human CD20; and (15) an anti-idiotypic antibody binding to the antibody cited above or to 2F2, 11B8 or 7D8.

BIOTECHNOLOGY - Preferred Antibody: The antibody is selected from an IgG1, an IgG2, an IgG3, an IgG4, an IgM, an IgA1, an IgA2, a secretory IgA, an IgD, and an IgE antibody. The antibody dissociates from human CD20 with a dissociation rate constant (kd) of about 10-5 seconds-1 or less. The antibody binds to human CD20 with an affinity constant (KD) of about 5 nM or less. It has one or more of the characteristics selected from: (a) capable of inducing complement dependent cytotoxicity (CDC) of cells expressing CD20 in the presence of complement; (b) capable of inducing CDC of cells expressing CD20 and high levels of CD55 and/or CD59 in the presence of complement; (c) capable of inducing apoptosis of cells expressing CD20; (d) capable of inducing antibody dependent cellular cytotoxicity (ADCC) of cells expressing CD20 in the presence of effector cells; (e) capable of inducing homotypic adhesion of cells which express CD20; (f) capable of translocating into lipid rafts upon binding to CD20; (g) capable of prolonging the survival of a subject having tumor cells which express CD20; (h) capable of depleting cells expressing CD20; and (i) capable of depleting cells expressing low levels of CD20 (CD20low

cells). Additionally, the antibody is: (a) capable of inducing at least 20%, and preferably at least 30% CDC mediated lysis of B-CLL cells in the presence of 33 vol/vol% plasma within 3 hours at 37degreesC at an antibody concentration of 10 mug/ml; (b) capable of inducing at least 20%, and preferably at least 30% lysis of B-CLL cells in the presence of 33 vol/vol% whole blood cells within 3 hours at 37degreesC at an antibody concentration of 10 mug/ml; (c) capable of prolonging the 50% survival rate of SCID mice injected with Daudi cells by more than 30% at a dose of 20 mug; or (d) capable of depleting peripheral B cells expressing low levels of CD20 (CD20 low B cells) to undetectable levels for more than 50 days in cynomolgus monkeys at a dosage of 6.25 mg/kg per day for 4 consecutive days. The antibody is capable of inducing at least 20%, and preferably at least 30% CDC mediated lysis of B-CLL cells in the presence of 33 vol/vol% plasma within 3 hours at 37 oC at an anti-CD20 antibody concentration of 10 mug/ml. The antibody is encoded by human heavy chain and human kappa light chain nucleic acids comprising nucleotide sequences in their variable regions as any of the 6 sequences of 382-433 bp fully defined in the specification, and conservative sequence modifications. It comprises a human heavy chain and human kappa light chain variable regions comprising any of the 6 sequences of 127-144 amino acids fully defined in the specification, or their modifications or homologues. The homologue comprises a sequence that is at least 90-99% homologous to the above amino acid sequences. The human monoclonal antibody: (a) does not comprise or require the amino acid residue proline at position 172; (b) does not comprise or require the amino acid residues alanine at position 170 or proline at position 172; (c) comprises or requires the amino acid residues asparagine at position 163 and asparagine at position 166; (d) does not comprise or require the amino acid residue proline at position 172, but which comprises or requires the amino acid residues asparagine at position 163 and asparagine at position 166; or (e) does not comprise or require the amino acid residues alanine at position 170 or proline at position 172, but which comprises or requires the amino acid residues asparagine at position 163 and asparagine at position 166. In addition, the human monoclonal antibody has one or more of the following characteristics: (a) binds to mutant P172S CD20 (proline at position 172 mutated to serine) with at least the same affinity as to human CD20; (b) binds to mutant AxP (alanine at position 170 mutated to serine, and proline at position 172 mutated to serine) with at least the same affinity as to human CD20; (c) shows a reduced binding of 50% or more to mutant N166D (asparagine at position 166 mutated to aspartic acid) compared to human CD20 at an antibody concentration of 10 mug/ml; or (d) shows a reduced binding of 50% or more to mutant N163D (asparagine at position 163 mutated to aspartic acid) compared to human CD20 at an antibody concentration of 10 mug/ml. The antibody binds to an epitope in the small first extracellular loop of human CD20 or to a discontinuous epitope on CD20. The epitope comprises part of the first small extracellular loop and part of the second extracellular loop. It has residues AGIYAP of the small first extracellular loop and residues MESLNFIRAHTPYI of the second extracellular loop. The antibody comprises at least one CDR sequence selected from: (a) any of the 18 amino acid sequences of 6-17 amino acids fully defined in the specification; (b) conservative sequence modifications of the sequences listed in (a); and (c) fragments of any one of the sequences (a) or (b) which retain the ability to bind to human CD20. The sequences comprise at least one amino acid substitution, deletion or addition of the sequence of the above-mentioned amino acid sequences. The antibody is an intact antibody that is glycosylated in a eukaryotic cell. It is an antibody fragment or a single chain antibody. The binding-domain immunoglobulin fusion protein comprises: (i) a binding domain polypeptide in the form of a heavy chain variable region or a light chain variable region that is fused to an immunoglobulin hinge region polypeptide; (ii) an immunoglobulin heavy chain CH2 constant region fused to the hinge region; and (iii) an immunoglobulin heavy chain

CH3 constant region fused to the CH2 constant region. The antibody is produced by a hybridoma which includes a B cell obtained from the above transgenic non-human animal, or by a transfectoma comprising nucleic acids encoding a human heavy chain and a human light chain. It comprises a heavy chain variable region amino acid sequence derived from a human VH3-13/DP-44 germline sequence (S54) or VH3-09/JH6b germline sequence (S56), and a light chain variable region amino acid sequence derived from a human L6/JK4-CK (S55) or VL-L6/JK5 (S57) germline sequence. Preferred Method: Producing a human monoclonal antibody which binds to human CD20, comprises immunizing a transgenic non-human animal having a genome comprising a human heavy chain transgene and a human light chain transgene with human CD20 or a cell expressing human CD20, such that antibodies are produced by B cells of the animal; isolating B cells of the animal; fusing the B cells with myeloma cells to form immortal, hybridoma cells that secrete human monoclonal antibodies specific for human CD20; and isolating the human monoclonal antibodies specific for CD20 from the culture supernatant of the hybridoma, or the transfectoma derived from such hybridoma. The immunization is performed with cells that have been transfected with human CD20. Inhibiting growth of a cell expressing CD20 comprises contacting the cell with an amount of the antibody such that the growth of the cell is inhibited. The method also applies in killing a cell expressing CD20. The cell is a B lymphocyte or a tumor cell. Treating or preventing a disease or disorder involving cells expressing CD20, comprises administering to a subject the above human antibody, composition, immunoconjugate, bispecific molecule or expression vector in an amount to treat or prevent the disease. The disease is a B cell lymphoma or a B cell non-Hodgkin's lymphoma. The disease is selected from precursor B cell lymphoblastic leukemia/lymphoma and mature B cell neoplasms, such as B cell chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL), B cell prolymphocytic leukemia, lymphoplasmacytic lymphoma, mantle cell lymphoma (MCL), follicular lymphoma (FL), cutaneous follicle center lymphoma, marginal zone B cell lymphoma (MALT type, nodal and splenic type), hairy cell leukemia, diffuse large B cell lymphoma, Burkitt's lymphoma, plasmacytoma, plasma cell myeloma, post-transplant lymphoproliferative disorder, Waldenstrom's macroglobulinemia and anaplastic large-cell lymphoma (ALCL). The disease is also selected from lymphomatoid granulomatosis, primary effusion lymphoma, intravascular large B cell lymphoma, mediastinal large B cell lymphoma, heavy chain diseases (including gamma, mu and alpha disease), lymphomas induced by therapy with immunosuppressive agents, such as cyclosporine-induced lymphoma, and methotrexate-induced lymphoma. The treatment includes the killing of B cells which produce antibodies against autoantigens. The disorder may also include psoriasis, psoriatic arthritis, dermatitis, systemic scleroderma and sclerosis, inflammatory bowel disease (IBD), Crohn's disease, ulcerative colitis, respiratory distress syndrome, meningitis, encephalitis, uveitis, glomerulonephritis, eczema, asthma, atherosclerosis, leukocyte adhesion deficiency, multiple sclerosis, Raynaud's syndrome, Sjogren's syndrome, juvenile onset diabetes, Reiter's disease, Behcet's disease, immune complex nephritis, IgA nephropathy, IgM polyneuropathies, immune-mediated thrombocytopenias, such as acute idiopathic thrombocytopenic purpura and chronic idiopathic thrombocytopenic purpura, hemolytic anemia, myasthenia gravis, lupus nephritis, systemic lupus erythematosus, rheumatoid arthritis (RA), atopic dermatitis, pemphigus, Graves' disease, Hashimoto's thyroiditis, Wegener's granulomatosis, Omenn's syndrome, chronic renal failure, acute infectious mononucleosis, HIV, and herpes virus associated diseases. The autoimmune disease is rheumatoid arthritis. The method further comprises separately administering another therapeutic agent to the subject. The therapeutic agent is a cytotoxic agent or a radiotoxic agent, an immunosuppressant, an immunological modulating agent (e.g. a cytokine or a chemokine), or doxorubicin, cisplatin, bleomycin, carmustine, chlorambucil and cyclophosphamide. In addition, the therapeutic agent is selected from anti-CD25 antibodies, anti-CD 19 antibodies,

anti-CD21 antibodies, anti-CD22 antibodies, anti-CD37 antibodies, anti-CD38 antibodies, anti-IL6R antibodies, anti-IL8 antibodies, anti-IL15 antibodies, anti-IL15R antibodies, antiCD4 antibodies, anti-CD11a antibodies, anti-alpha-4/beta-1 integrin (VLA4) antibodies, CTLA4-Ig, and anti-C3b(i) antibodies. The in vitro method for detecting the presence of CD20 antigen, or a cell expressing CD20, in a sample comprises contacting the sample with the above antibody under conditions that allow for formation of a complex between the antibody and CD20; and detecting the formation of a complex. The in vivo method for detecting CD20 antigen, or a cell expressing CD20, in a subject comprises administering the antibody under conditions that allow for formation of a complex between the antibody and CD20; and detecting the formed complex. Preferred Composition: The composition comprises a first antibody and a second antibody. It further comprises a therapeutic agent or a chelator linker for attaching a radioisotope.

ACTIVITY - Cytostatic; Antipsoriatic; Antiinflammatory; Neuroprotective; Ophthalmological; Nephrotropic; Antiasthmatic; Antiarteriosclerotic; Antianemic; Antirheumatic; Antiarthritic; Antithyroid; Anti-HIV. No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The composition and methods are useful for diagnosing, preventing or treating diseases or disorders involving cells expressing CD20, such as cancer, psoriasis, inflammatory bowel disease, meningitis, uveitis, glomerulonephritis, asthma, atherosclerosis, multiple sclerosis, hemolytic anemia, myasthenia gravis, rheumatoid arthritis, Graves' disease or HIV. The anti-idiotypic antibody is used for detecting the level of human monoclonal antibody against CD20 in a sample (claimed).

ADMINISTRATION - Weekly dosages may range from about 250-2000 mg. Administration can be oral, nasal, topical, rectal, vaginal and/or parenteral.

EXAMPLE - No relevant example given. (201 pages)

L4 ANSWER 9 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2003:907356 CAPLUS

DN 141:104816

TI Monoclonal Antibodies in the Treatment of Chronic Lymphoid Leukemias

AU Robak, Tadeusz

CS Copernicus Memorial Hospital, Department of Hematology, Medical University of Lodz, Lodz, 93-513, Pol.

SO Leukemia & Lymphoma (2004), 45(2), 205-219

CODEN: LELYEA; ISSN: 1042-8194

PB Taylor & Francis Ltd.

DT Journal; General Review

LA English

AB A review. In recent years preclin. and clin. studies have been undertaken with selected monoclonal antibodies (MoAbs) either alone or conjugated to toxins in patients with several lymphoid malignancies, including chronic lymphocytic leukemia (CLL), prolymphocytic leukemia (PLL) and hairy cell leukemia (HCL). Two MoAbs, directed against CD20 antigen (Rituximab, RIT) and CD52 antigen (Campath-1H, alemtuzumab, ALT) demonstrate significant activity in CLL. The most notable success to date has been achieved with ALT, both in previously treated and untreated patients with CLL. ALT is a humanized rat IgG1 antibody that binds to the cell membrane of virtually all normal as well as malignant lymphocytes. In the vast majority of CLL patients ALT causes constant reduction of abnormal blood lymphocytes, usually

in

less than 4 wk, and disappearance of CD5/CD19 co-expression cells from blood. The regression of lymphoid infiltration from other sites is less clear. ALT is also highly active in patients with CLL in progression, even refractory to fludarabine (FA). Hematol. toxicity, especially

long-lasting

lymphocytopenia, was noted in the majority of patients. The most important clin. side effects of ALT treatment were infections, mainly

herpes simplex virus and cytomegalovirus reactivation. RIT is also active in CLL in conventional doses. However some studies suggest that higher doses are more effective than standard doses, used routinely in other lymphoid malignancies. The activity of ALT and RIT in CLL patients resistant to FA and their synergistic interactions with cytotoxic drugs suggests that a combination of these agents may lead to further progress in the treatment of this disease. The T-cell variant of PLL has demonstrated impressive responses to ALT in several trials even if the patients were refractory to deoxycoformycin (DCF) and other agents. However, this MoAb is not curative, because all patients eventually relapsed. Consequently, treatment with ALT may need to be associated with stem cell transplantation to consolidate and maintain long-term remissions. Recently anti-CD22 and anti-CD25 immunotoxins have been investigated in purine analogs refractory or relapsed HCL. The presented results indicate that these agents are highly active and well tolerated even if the patients were resistant to 2-CdA or DCF.

RE.CNT 108 THERE ARE 108 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:777108 CAPLUS
DN 139:306535
TI Human IgM antibodies for drug screening, diagnostic, therapeutic uses
against central nervous system diseases
IN Rodriguez, Moses; Miller, David J.; Pease, Larry R.
PA Mayo Foundation, USA
SO U.S. Pat. Appl. Publ., 159 pp., Cont.-in-part of U.S. Ser. No. 730,473.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003185827	A1	20031002	US 2001-10729	20011113
	US 5591629	A	19970107	US 1994-236520	19940429
	US 2002164325	A1	20021107	US 1997-779784	19970107
	US 2006140930	A1	20060629	US 2005-224664	20050912
PRAI	US 1994-236520	A2	19940429		
	US 1996-692084	A1	19960808		
	US 1997-779784	A2	19970107		
	US 1999-322862	B2	19990528		
	US 2000-580787	B2	20000530		
	US 2000-730473	A2	20001205		

AB Antibodies, and particularly human antibodies, are disclosed that demonstrate activity in the treatment of demyelinating diseases as well as other diseases of the central nervous system that are of viral, bacterial or idiopathic origin, including neural dysfunction caused by spinal cord injury. Neuromodulatory agents are set forth that include and comprise a material selected from the group consisting of an antibody capable of binding structures or cells in the central nervous system, a peptide analog, a hapten, active fragments thereof, agonists thereof, mimics thereof, monomers thereof and combinations thereof. The neuromodulatory agent has one or more of the following characteristics: it is capable of inducing remyelination; binding to neural tissue; promoting Ca ++ signaling with oligodendrocytes; and promoting cellular proliferation of glial cells. Amino acid and DNA sequences of exemplary antibodies are disclosed. Methods are described for treating demyelinating diseases, and diseases of the central nervous system of humans and domestic animals, using polyclonal IgM antibodies and human monoclonal antibodies sHIgM22(LYM 22), sHIgM46(LYM46), ebvHIgM MSI19D10, CB2bG8, AKJR4, CB2iE12, CB2iE7, MSI19E5 and MSI10E10, active fragments thereof and the like. The invention also extends to the use of human antibodies, fragments, peptide derivs. and like materials, and their use in diagnostic and therapeutic applications, including screening assays for

the discovery of addnl. antibodies that bind to cells of the nervous system, particularly oligodendrocytes.

L4 ANSWER 11 OF 42 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2004-03435 BIOTECHDS
TI Purifying target protein from mixture containing host cell protein involves subjecting mixture to non-affinity purification, high-performance tangential flow filtration and isolating purified protein;
antibody and fusion protein production for use in diagnosis and therapy
AU FAHNER R L; FOLLMAN D; LEBRETON B; VAN REIS R
PA GENENTECH INC
PI WO 2003102132 11 Dec 2003
AI WO 2003-US13054 25 Apr 2003
PRAI US 2002-375953 26 Apr 2002; US 2002-375953 26 Apr 2002
DT Patent
LA English
OS WPI: 2004-043096 [04]
AN 2004-03435 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Purifying (M1) a target protein from a mixture containing a host cell protein, comprising subjecting the mixture to a non-affinity purification followed by high-performance tangential flow filtration (HPTFF) and isolating the protein in a purity containing less than 100 parts/million (ppm) of the host cell protein, where (M1) includes no affinity purification process, is new.
BIOTECHNOLOGY - Preferred Method: In (M1), a non-affinity purification process includes a first and second non-affinity purification process. The first and second non-affinity purification processes are different and chosen from ion exchange chromatography and hydrophobic interaction chromatography, where ion exchange chromatography is chosen from cation exchange chromatography, anion exchange chromatography and mixed mode ion exchange chromatography. The cation exchange chromatography process is performed on a cation exchange ligand chosen from carboxy methyl, BAKERBOND ABX (RTM), sulfopropyl (SP), and sulfonyl or performed on a cation exchange resin chosen from carboxy methyl-cellulose, BAKERBOND ABX (RTM), sulfopropyl immobilized on agarose and sulfonyl immobilized on agarose. The anion exchange ligand is chosen from the DEAE and quaternary ammonium ions or chosen from diethylaminoethyl (DEAE) cellulose, QAE SEPHADEX (RTM) and FAST SEPHAROSE (RTM). The HPTFF is performed using a charged membrane. The host cell protein is Chinese hamster ovary protein (CHOP). The target protein is an antibody, or immunoadhesin, where the antibody is a monoclonal antibody, polyclonal antibody, humanized antibody, human antibody, or antibody fragment which is chosen from Fab, Fab', F(ab')₂ and Fv fragments, single-chain antibody molecules, diabodies, linear antibodies, bispecific antibodies and multispecific antibodies formed from antibody fragments. The antibody specifically binds to an antigen chosen from CD3, CD4, CD8, CD19, CD20, CD34, CD40, epidermal growth factor (EGF) receptor, HER2, HER3, HER4 receptor, LFA-1, Mac1, p150,95, VLA-4, ICAM-1, VCAM, av/b3 integrin, CD11a, CD18, CD11b, VEGF, IgE, flk2/flt3 receptor, obesity (OB) receptor, mpl receptor, cytotoxic T-lymphocyte associated antigen (CTLA)-4 and polypeptide C, where the antibody is chosen from anti-HER2, anti-CD20, anti-IL-8, anti-VEGF, anti-PSCA, anti-CD11a, anti-IgE, anti-Apo-2 receptor, anti-TNF-alpha, anti-tissue factor (TF), anti-CD3, anti-CD25, anti-CD34, anti-CD40, anti-tac, anti-CD4, anti-CD52, anti-Fc receptor, anti- carcinoembryonic antigen (CEA) antibodies, antibodies directed against breast epithelial cells, antibodies that bind to colon carcinoma cells, anti-CD33, anti-CD22, anti-EpCAM, anti-GpIIb/IIIa, anti-RSV, anti-CMV, anti-HIV, anti-hepatitis, anti-alphavbeta3, anti-human renal cell carcinoma, anti-human 17-1A, anti-human colorectal tumor, anti-human melanoma, anti-human squamous cell carcinoma, and anti-human leukocyte antigen

(HLA) antibodies. The target protein is an antibody-like molecule, which is a protein fused to or conjugated with, a CH2/CH3 region. The protein is chosen from renin, growth hormones, growth hormone releasing factor, parathyroid hormone, thyroid stimulating hormone, lipoproteins, alpha-1 antitrypsin, insulin A-chain, insulin B-chain, proinsulin, follicle stimulating hormone, calcitonin, luteinizing hormone, glucagon, factor VIIIC, factor IX, tissue factor, Von Willebrands factor, protein C, atrial natriuretic factor, lung surfactant, urokinase, human urine and tissue type plasminogen activator (t-PA), bombesin, thrombin, hemopoietic growth factor, tumor necrosis factor alpha and beta, enkephalinase, regulated on activation normally T-cell expressed and secreted (RANTES), human macrophage inflammatory protein (MIP-1-alpha), serum albumins, Muellerian-inhibiting substance, relaxin A-chain, relaxin B-chain, prorelaxin, mouse gonadotropin-associated peptides, beta-lactamase, DNase, IgE, CTLAs, inhibin, activin, vascular endothelial growth factor (VEGF), receptors for hormones or growth factors, protein A or D, rheumatoid factors, bone-derived neurotrophic factor (BDNF), neurotrophin-3, -4, -5 and -6 (NT-3, NT-4, NT-5 and NT-6), nerve growth factors, platelet-derived growth factor (PDGF), fibroblast growth factors, EGF, transforming growth factors (TGF), insulin-like growth factor-I and -II (IGF-1 and IGF-II), des(1-3-IGF-I (brain IGF-1), insulin-like growth binding protein (IGFBPs), CD proteins, erythropoietin, osteoinductive factors, immunotoxins, bone morphogenetic proteins (BMPs), interferons-alpha, -beta, -gamma, colony stimulating factors (CSFs), interleukins IL-1 to IL-10, superoxide dismutase, T-cell receptors, surface membrane proteins, decay accelerating factor, viral antigens, transport proteins, homing receptors, addressins, regulatory proteins, integrins, and tumor-associated antigens and its fragments. (M1) further involves incorporating the isolated protein into a pharmaceutical formulation.

USE - (M1) is useful for purifying a target protein from a mixture containing a host cell protein and useful for incorporating the isolated protein into a pharmaceutical formulation (claimed). Purified protein is useful in pharmaceutical and also useful in various diagnostic and therapeutic purposes.

ADVANTAGE - (M1) is efficient in purifying a target protein from a mixture containing a host cell protein. (M1) effectively performed at low cost.

EXAMPLE - Combination of non-affinity chromatography and high-performance tangential flow filtration (HPTFF) was performed for the purification of anti-CD40 recombinant human monoclonal antibody, anti-CD40 rhuMAb, with a molecular weight of 160 kDa and pI of 9.3 from Chinese Hamster Ovary (CHO) cells as follows. The anti-CD40 rhuMAb was obtained from an industrial scale CHO cell culture. After CHO cell culture, the anti-CD40 rhuMAb molecule was partially clarified by centrifugation and normal cell filtration was performed to remove cells and cell debris. The resulting pool consisted of 1.7 mg/ml of anti-CD40 rhuMAb product and approximately 0.4 mg/ml of Chinese Hamster Ovary Protein (CHOP). For purification of anti-CD40 rhuMAb, conditioned harvested cell (HCCF) comprising anti-CD40 rhuMAb product and CHOP from CHO cells expressing anti-CD40 rhuMAb was loaded in cation exchange chromatography column (S) to remove host cell proteins or CHOP, variants, DNA impurities and aggregates. Elutions from the S column were pooled and subjected to a second anion exchange chromatography column (Q) Q-SEPHAROSE FAST FLOW (RTM) resin to remove CHOP, DNA impurities and target protein aggregates. The flow-through from the Q column was further subjected to a third process of HPTFF for further removal of CHOP, variants and small molecules. The amount of anti-CD40 rhuMAb in each pool following a purification process i.e. in the HCCF and in the pools from the purification process, was determined by an high performance liquid chromatography (HPLC) analysis based on protein-A immunoaffinity. CHOP concentration was determined using the enzyme-linked immunosorbent (ELISA) assay. The HPTFF experiment purification process using a positively charged CRC300+ membrane was begun by first concentrating the

substance from the Q pool until the bulk volume reached a bulk concentration (Cb) of 10 g/l. The resultant solution in the recycle tank was then subjected to sequential diafiltration process and the yield was calculated based on the quantifiable product sieving during diafiltration. Significant sieving of CHOP was observed with positively charged CRC300+HPTFF membrane without any significant loss of positively charged anti-CD40 rhuMab. CHOP removal occurred during both concentration diafiltration. The CHOP concentration was reduced from 15 parts per million (ppm) (concentration in a substance recovered from the Q chromatography column) to less than 0.6 ppm within the first 20 diavolumes (concentration in the protein pool in the recycle tank). The removal of CHOP impurities was confirmed by measuring the concentration in the substance recovered from the HPTFF experiment and no significant filtrate losses were observed. Thus, purified anti-CD40 rhuMab was obtained. (77 pages)

L4 ANSWER 12 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:145016 CAPLUS
DN 138:302181
TI Inolimomab OPi
AU Winkler, Michael
CS Klinik fuer Visceral- und Transplantationschirurgie, Medizinische Hochschule Hannover, Hannover, 30625, Germany
SO Current Opinion in Investigational Drugs (PharmaPress Ltd.) (2002), 3(10), 1464-1467
CODEN: COIDAZ; ISSN: 1472-4472
PB PharmaPress Ltd.
DT Journal; General Review
LA English
AB A review. OPi (formerly Orphan Pharma International) is developing inolimomab, an anti-interleukin-2 receptor (CD25) monoclonal antibody for the potential treatment of acute graft vs. host disease [405003], [405020], [464860]. As of Apr. 2001, inolimomab was undergoing phase II/III clin. trials [405210].
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:66193 CAPLUS
DN 138:147065
TI Advances in the management of psoriasis: monoclonal antibody therapies
AU Mehrabi, Don; DiCarlo, Joshua B.; Soon, Seaver L.; McCall, Calvin O.
CS Department of Dermatology, Emory University School of Medicine, Atlanta, GA, 30322, USA
SO International Journal of Dermatology (2002), 41(12), 827-835
CODEN: IJDEBB; ISSN: 0011-9059
PB Blackwell Science Ltd.
DT Journal; General Review
LA English
AB A review. Psoriasis is a common skin disorder characterized by erythematous, scaling plaques. Until recently, therapies for this disease have been aimed at reducing keratinocyte proliferation. We have learned that psoriasis is not primarily a disorder of keratinocyte hyperproliferation, but is an inflammatory disease. This knowledge, especially our current understanding of the role of activated T cells in psoriasis, has led to new therapeutic options and new areas of research. Immunosuppressive agents such as cyclosporine have proven very useful in the treatment of psoriasis, but their use is limited by toxicity. Monoclonal antibodies directed against key components of the inflammatory process have been studied in an attempt to produce safer, more selective immunosuppressive agents. This review summarizes much of the available literature describing the use of monoclonal antibodies in the treatment of psoriasis.
RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:404364 CAPLUS
DN 138:88023
TI The utility of monoclonal antibody therapy in renal transplantation
AU Loertscher, R.
CS Division of Transplantation, McGill University Health Centre, Montreal, QC, Can.
SO Transplantation Proceedings (2002), 34(3), 797-800
CODEN: TRPPA8; ISSN: 0041-1345
PB Elsevier Science Inc.
DT Journal; General Review
LA English
AB A review discusses the clin. experience with the therapeutic use of monoclonal antibodies (MAbs), including OKT3, in renal transplantation. OKT3 provided a considerably higher rejection reversal rate and efficacious in controlling corticosteroid-resistant rejection episodes. The interaction of OKT3 with target T lymphocytes was reproducibly associated with febrile illness, and sometimes, with diarrhea, pulmonary edema, and/or a meningitis-like syndrome. Two molecularly engineered MAbs with specificity for the CD25 receptor chain were developed, daclizumab and basiliximab, to address the issues of clin. tolerance and therapeutic usefulness. Daclizumab and basiliximab were well-tolerated and completely devoid of clin. symptoms that could be related to the antibody. The clin. tolerance of daclizumab and basiliximab was significant for the complete absence of symptoms that could be attributed to the injections of these antibodies.

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:833383 CAPLUS
DN 135:370639
TI Human IgM antibodies with the capability of inducing remyelination, and diagnostic and therapeutic uses thereof particularly in the central nervous system
IN Rodriguez, Moses; Miller, David J.; Pease, Larry R.
PA Mayo Foundation for Medical Education & research, USA
SO PCT Int. Appl., 219 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001085797	A1	20011115	WO 2000-US14902	20000530
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2409515	AA	20011115	CA 2000-2409515	20000530
	EP 1294770	A1	20030326	EP 2000-948498	20000530
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	BR 2000015875	A	20030624	BR 2000-15875	20000530
	JP 2004516807	T2	20040610	JP 2001-582396	20000530
PRAI	US 2000-568351	A2	20000510		
	WO 2000-US14902	W	20000530		

AB Methods are described for treating demyelinating diseases in mammals, such as multiple sclerosis in humans, and viral diseases of the central nervous system of humans and domestic animals, such as post-infectious encephalomyelitis, or prophylactically inhibiting the initiation or progression of demyelination in these disease states, using human monoclonal autoantibodies characterized by their ability to bind structures and cells within the central nervous system. In particular, the methods utilize human monoclonal antibodies selected from the group of sHlgM22 (LIM 22), sHlgM46 ebvHlgM MSI19D10, CB2bG8, AKJR4, CB2iE12, CB2iE7 and MSI 19E5, monomers thereof, active fragments thereof and isolated or synthetic human or humanized autoantibodies having the characteristics of the foregoing. Nucleic acids and DNA mols. encoding the human monoclonal antibodies, or portions thereof, are provided. The invention also extends to the preparation and use of human polyclonal and monoclonal autoantibodies, monomers thereof, active fragments, peptide derivs. and fragments, and analogs, cognates, agonists and the like corresponding materials, and their use in diagnostic and therapeutic applications. For example, the autoantibodies, monomers, fragments, haptens, and peptide equivalent, are useful in the promotion of neural regeneration and neuroprotection, and therapeutic compns. and vaccines containing peptides or antibodies are included and presented.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2001:881772 CAPLUS

DN 136:338992

TI Monoclonal antibodies in oncology

AU Baryshnikov, A. Yu.; Polosukhina, E. R.

CS NII Eksp. Diagnostiki i Terapii Opukholei, RONTs im. N. N. Blokhina, RAMN, Moscow, Russia

SO Vestnik Rossiiskoi Akademii Meditsinskikh Nauk (2001), (9), 14-18

CODEN: VAMEE3; ISSN: 0869-6047

PB Izdatel'stvo Meditsina

DT Journal; General Review

LA Russian

AB A review. Explorations into hybridoma technologies at the N. N. Blokhin Russian Cancer Research Center were started in the late 1970s. ICO series monoclonal antibodies (MAb) against different human differentiation leukocyte antigens have been designed in a short period of time. MAb to antigens CD25, CD8, CDw50, CD5, CD4, CD7, CD3, CD71, CD34, CD45, CD38, CD11b, CD16, and CD95 have gained worldwide recognition at International HLA Workshop Conferences. Today, the collection of hybridomas at the Center includes more than 200 samples. MAb are used for immunophenotypic assays of blood and bone marrow cells, for classification of lymphomas and leukemias, and for assessment of human immunity for immunophenotypic diagnosis of minimal residual tumor in multiple myeloma. New prognostic markers in various nosol. entities and MAb biol. activity are under study. MAb have been used to develop ELISA diagnostic kits. They are employed as vectors for immunotoxin design, for immunomagnetic separation, and many MAb-based drugs have been designed. A start has been made on the promising development of a new line of biopharmaceutics, namely design of new immunoliposomal dosage forms of doxorubicin and betulinic acids.

L4 ANSWER 17 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2000:896140 CAPLUS

DN 135:59898

TI An early experience with Simulect (basiliximab): an IL-2 receptor antibody

AU Hinduja, A.; Abraham, G.; Eapen, G.; Shroff, S.; Rao, R.; Kuruvilla, S.

CS Sri Ramachandra Medical College, Porur, Chennai, India

SO Transplantation Proceedings (2000), 32(7), 1739-1740

CODEN: TRPPA8; ISSN: 0041-1345

PB Elsevier Science Inc.

DT Journal

LA English

AB Early acute rejection episodes have an overriding effect on allograft survival. The goal, therefore, is to decrease acute rejection episodes by using immunosuppressive agents with greater efficacy and minimal toxicity. Used sparingly in developing countries owing to its prohibitive costs, induction therapy with Simulect (basiliximab) provides augmented immunosuppression in the post-transplant period. Experience with this chimeric (mouse and human) monoclonal antibody in four renal transplant recipients, is described. Findings showed that basiliximab reduces the incidence of acute rejection episodes and has fewer serious adverse effects when compared to other monoclonal and polyclonal antibodies. However, the prohibitive cost and nonavailability of this IL-2 receptor antibody makes its use in developing countries rare.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2

AN 2000:869248 CAPLUS

DN 134:160500

TI Lipopolysaccharide-dependent induction of leech leukocytes that cross-react with vertebrate cellular differentiation markers

AU de Equileor, M.; Grimaldi, A.; Tettamanti, G.; Valvassori, R.; Cooper, E. L.; Lanzavecchia, G.

CS DBSF, University of Insubria, Varese, 21100, Italy

SO Tissue & Cell (2000), 32(5), 437-445

CODEN: TICEBI; ISSN: 0040-8166

PB Harcourt Publishers Ltd.

DT Journal

LA English

AB The authors have designed expts. to characterize leech leukocytes that mediate inflammatory responses. Shortly after inflicting injury to the body wall in the presence of lipopolysaccharides, many cells resembling macrophages, NK cells and granulocytes of vertebrates and many invertebrates migrated to the lesioned area. Nuclei of migrating cells incorporated bromodeoxyuridine. Using human monoclonal antibodies, macrophage-like cells were pos. for CD25, CD14, CD61, CD68, CD11b and CD11c. NK-like cells were pos. for CD25, CD56, CD57 and CD16, and granulocytes were pos. for CD11b and CD11c. In blots of leech expts., the CD25 monoclonal antibody recognized a band of about 55 kDa; the CD56 monoclonal antibody, two bands of about 140 and 210 kDa; the CD57 monoclonal antibody, two bands of about 106 and 70 kDa; the CD14 monoclonal antibody, a band of about 50 kDa; the CD16 monoclonal antibody, a band of about 60 kDa.. CD61 and CD68 both recognized a band of about 110 kDa; CD11b recognized a band of 200 kDa, and CD11c, a band of 180 kDa..

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1996:101796 CAPLUS

DN 124:143145

TI Human and humanized monoclonal antibodies: preclinical studies and clinical experience

AU Ostberg, L.; Queen, C.

CS Protein Design Labs., Inc., Mountain View, CA, 94043, USA

SO Biochemical Society Transactions (1995), 23(4), 1038-43

CODEN: BCSTB5; ISSN: 0300-5127

PB Portland Press

DT Journal

LA English

AB Human monoclonal antibodies were prepared by using human + (mouse + human) heterohybridomas. Humanized antibodies have concentrated on reagents against human antigens, when suitable human antibodies would be difficult to obtain. Examples are humanized antibody binding to the p55 chain of the IL-2 receptor, anti-CD33, and those to viruses. Human monoclonal antibodies to hepatitis B surface antigen have been used in prophylactic studies.

L4 ANSWER 20 OF 42 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 1996-02724 BIOTECHDS
TI Human and humanized monoclonal antibodies: preclinical studies and clinical experience;
monoclonal antibody engineering for humanized antibody construction, and human monoclonal antibody production
(conference paper)

AU Oestberg L; Queen C
CS Protein-Des.Labs
LO Protein Design Labs, Inc., 2375 Garcia Avenue, Mountain View, CA 94043, USA.
SO Biochem.Soc.Trans.; (1995) 23, 4, 1038-43
CODEN: 9996F
Adventures with Membrane Lipids, 655th Meeting, Manchester, UK, 18-21 July, 1995.

DT Journal

LA English

AN 1996-02724 BIOTECHDS

AB To obtain humanized antibodies (hAbs), a human framework was chosen that had the highest possible homology to the original mouse antibody, and computer modeling was used to identify amino acids from the mouse framework that might interact with the complementarity determining regions or directly with the antigen, and these murine amino acids were retained. Programs involving hAbs have concentrated on reagents against human antigens, for which suitable human antibodies are difficult to obtain. 2 Of the hAbs developed are in clinical trials: humanized anti-Tac, which is directed to the interleukin-2 receptor on activated human T-lymphocytes; and humanized M195, which is targeted to the CD33 determinant on certain human myeloid precursor cells. In addition of hAbs, human monoclonal antibodies (hMAbs) have been obtained through the construction of human x (mouse x human) heterohybridomas (triomas). hMAbs have been produced against cytomegalo virus and hepatitis B virus antigens. The goal is to produce antibodies that are potent, specific, reproducible and non-immunogenic, have long in vivo half-lives and are free of unspecific toxicities. (45 ref)

L4 ANSWER 21 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3
AN 1995:447237 CAPLUS
DN 122:211416
TI Future of monoclonal antibodies in solid organ transplantation
AU Cosimi, A. Benedict
CS Department Surgery, Massachusetts General Hospital, Boston, MA, 02114, USA
SO Digestive Diseases and Sciences (1995), 40(1), 65-72
CODEN: DDSCDJ; ISSN: 0163-2116

DT Journal; General Review

LA English

AB A review with 25 refs. The ultimate objective of immunosuppressive therapy is to block transplant recipient reactivity to allograft incompatibilities while sparing other responses. Increased clarification of rejection mechanisms has made possible the precise suppression of specific elements of the immune response using murine anti-human monoclonal antibodies. In addition, recombinant DNA technol. has made available novel agents including "humanized," bispecific, or toxin-conjugated mols., which avoid some of the limitations of murine reagents. Using such agents, donor-specific tolerance has been

induced in exptl. models after a limited course of therapy directed against selected effector cell surface-associated mols. such as CD4, CD25, and CD54.

L4 ANSWER 22 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1994:296257 CAPLUS

DN 120:296257

TI Characterization of Humanized Anti-TAC, an Antibody Directed Against the Interleukin 2 Receptor, Using Electrospray Ionization Mass Spectrometry by Direct Infusion, LC/MS, and MS/MS

AU Lewis, Derf A.; Guzzetta, Andrew W.; Hancock, William S.; Costello, Maureen

CS Genentech Inc., South San Francisco, CA, 94080-4990, USA

SO Analytical Chemistry (1994), 66(5), 585-95

CODEN: ANCHAM; ISSN: 0003-2700

DT Journal

LA English

AB Characterization of a humanized monoclonal antibody (Hu-anti-TAC) directed against a surface protein expressed on T-lymphocytes was performed with an electrospray mass spectrometer. Capillary reversed-phase liquid chromatog. (LC)/mass spectrometry (MS) and direct infusion MS were utilized along with tandem MS/MS anal. to confirm the sequence and to determine the sources of heterogeneity in Hu-anti-TAC. The MS anal. was performed on disulfide-reduced and trypsin-digested samples of the antibody. Two forms of diantennary carbohydrate structures were identified and found to be consistent with those reported for the human IgG1 framework. The anal. demonstrated that the N-terminus was modified by conversion of a glutamine residue to pyroglutamic acid. Another source of heterogeneity was the partial removal of the C-terminal lysine residue and was confirmed by mass calcns. of tryptic peptides followed by MS/MS sequencing. The high sensitivity of electrospray mass spectrometry when combined with capillary chromatog. can allow detailed characterization of microgram samples of high mol. weight proteins such as antibodies.

L4 ANSWER 23 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1994:242080 CAPLUS

DN 120:242080

TI Inhibition of protein kinase C in PHA-activated PBMC treated with anti-HLA class I monoclonal antibody is associated to decreased proliferation and expression of cell cycle related genes

AU Rita, Selvatici; Michele, Rubini; Patrizia, Orlando; Alessandsra, Balboni; Sara, Boninsegna; Enrico, Gandini

CS Inst. Med. Genet., Univ. Ferrara, Ferrara, Italy

SO Biochemistry and Molecular Biology International (1994), 32(1), 105-14

CODEN: BMBIES; ISSN: 1039-9712

DT Journal

LA English

AB Treatment of PHA-activated PBMC with anti-HLA class I monoclonal antibody (mAb 01.65) shows: (1) depletion of particulate protein kinase C (PKC) and partial reduction of cytosolic PKC after only 10 min.; (2) inhibition of tritiated thymidine (3H-Td) incorporation; (3) slowing down of cell cycle; (4) reduced expression of four cell cycle related genes. These findings suggest that the depletion of PKC is reflected on the cell cycle progression and expression of cell cycle related genes. The authors studied, in PHA-activated PBMC cultures, the effect of N-N-Staurosporine (StSp) acting as PKC inhibitor at nanomolar concns., alone and combined with mAb 01.65. StSp, inhibits the proliferative response of PHA stimulated PBMC in a competitive fashion with mAb 01.65. The authors report here that StSp alone and combined with mAb 01.65 affects also the expression of c-myc and cdc2 and the membrane expression of two proliferation markers: IL-2R (CD25) and Tfr (CD71).

L4 ANSWER 24 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1994:293602 CAPLUS
 DN 120:293602
 TI Monoclonal WB B-cell line
 IN Wee, Richard K.
 PA Can.
 SO Can. Pat. Appl., 11 pp.
 CODEN: CPXXEB
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CA 2114311	AA	19930526	CA 1991-2114311	19911125
	CA 2114311	C	19960227		
PRAI	CA 1991-2114311		19911125		

AB An Epstein-Barr virus-neg. human B-cell line (designed WB) was derived from peripheral blood mononuclear cells of a healthy 48 yr-old Chinese male by use of a serum-free defined medium. The WB cells can sustain autonomous growth and replication in semi-suspension culture in a protein-free RPMI 1640 basal medium. The WB cells expressed the CD19 and CD20 pan-B antigens, IgG, and activation markers DR, DQ, Leu 8, CD23, CD25, CD38, and CD71. The conditioned medium (CM) from WB cultures contained two novel proteins, i.e., a 21 kDa blood tumor necrosis factor (BTNF or TNF- γ) and a 53 KDa B-cell specific activator protein (BSAP). The availability of this cell line would allow easy purification of these important secretory proteins, and production of human monoclonal antibodies. Also, further study of the cell line may provide the answer as to how cancer cells could gain autonomy in a milieu of apoptosis.

L4 ANSWER 25 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1993:122616 CAPLUS

DN 118:122616

TI Dissection of the combining site in a humanized anti-Tac antibody

AU Glaser, Scott M.; Vasquez, Maximiliano; Payne, Philip W.; Schneider, William P.

CS Protein Des. Labs, Inc., Mountain View, CA, 94043, USA

SO Journal of Immunology (1992), 149(8), 2607-14

CODEN: JOIMA3; ISSN: 0022-1767

DT Journal

LA English

AB The genetically engineered humanized anti-Tac antibody (HAT) has been shown to bind the p55 chain of the human IL-2R with an affinity close to that of the murine anti-Tac. Although the HAT mol. contains all six mouse CDR, it was not known which, and to what extent, each of the CDR contributes to antigen binding. These questions were addressed by constructing a series of variant HAT antibodies, each substituting a single HAT CDR with a heterologous CDR. The association consts. of the variant HAT antibodies to p55 were determined by competitive binding anal. CDR 1 and 3 of the H chain and CDR 3 of the L chain are essential for maintaining binding. The remaining three CDR appear to be involved to a lesser degree.

L4 ANSWER 26 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1993:252906 CAPLUS

DN 118:252906

TI A monoclonal antibody (H227) recognizing a new epitope of 4F2 molecular complex associated with T cell activation

AU Nakao, Masanobu

CS Sch. Med., Kurume Univ., Kurume, 830, Japan

SO Kurume Igakkai Zasshi (1992), 55(12), 737-50

CODEN: KIZAAL; ISSN: 0368-5810

DT Journal

LA Japanese
AB A murine monoclonal antibody (H227 mAb) recognizing a new epitope of 4F2 mol. complex involved in T cell activation pathways was developed and characterized. Staining patterns of H227 mAb were the same to those of 4F2 mAb. Thus, monocytes, thymocytes, activated lymphocytes and all cultured cell lines from T-cell, B-cell, monocyte, and granulocyte were strongly pos., while resting peripheral blood lymphocytes were weakly pos., and granulocytes and platelets were neg. for H227 antigen (Ag). H227 Ag was induced on PHA-activated T cells much earlier than the other T-cell activation antigens such as transferrin receptor, IL-2 receptor (IL-2R), or HLA-DR. Both H227 and 4F2 mAbs immunopptd. the 125 kDa membrane protein under non-reducing condition, and 85 kDa heavy chain and 40 kDa light chain proteins under reducing condition. These 2 mAbs immunopptd. only 85 kDa heavy chain protein when cell lysate was initially treated with dithiothreitol. Sequential immunopptn. proved their cross-reactivity. Both H227 and 4F2 mAbs inhibited PHA-induced peripheral blood mononuclear cell (PBMC) proliferation. In contrast, H227 mAb augmented PMA-induced PBMC proliferation whereas 4F2 mAb did not. These H227 mAb-mediated modulations of T cell proliferation well correlated with IL-2R expression levels and also IL-2 production in the supernatants. In summary, H227 mAb recognizes a new epitope of 4F2 heavy chain that might be involved in PMA-induced T cell activation pathway.

L4 ANSWER 27 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1993:578915 CAPLUS

DN 119:178915

TI Combinatorial functions of two chimeric antibodies directed to human CD4 and one directed to the α -chain of the human interleukin-2 receptor

AU Weissenhorn, Winfried; Scheuer, Werner; Kaluza, Brigitte; Schwirzke, Marina; Reiter, Christian; Flieger, Dimitri; Lenz, Helmut; Weiss, Elisabeth H.; Rieber, Ernst Peter; et al.

CS Inst. Immunol., Univ. Muenchen, Munich, W-8000, Germany

SO Gene (1992), 121(2), 271-8

CODEN: GENED6; ISSN: 0378-1119

DT Journal

LA English

AB The general feasibility of chimerization of monoclonal antibodies (mAbs) has already been shown for a large number of them. In order to evaluate in vitro parameters relevant to immunosuppressive therapy, the authors have chimerized and synthesized 2 anti-CD4 mAbs recognizing 2 different epitopes on the human T-lymphocyte antigen, CD4. The chimerized mAbs are produced at levels corresponding to those of the original hybridoma cell lines. With respect to activation of human complement, the individual Abs are neg.; however, when used in combination, complement activation was performed. When applied in combination, they modulated the CD4 antigen, whereas the individual mAb do not display this property. Individually they mediate an $\leq 60\%$ inhibition of the mixed lymphocyte reaction (MLR). However, by combination of an anti-CD4 mAb with one directed against the α -chain of the human interleukin-2 (IL2) receptor, nearly 100% inhibition of the MLR was achieved, even with reduced dosage of the mAbs. Apparently, the combination of an anti-CD4 mAb and an anti-IL2R α chain mAb is more effective with respect to immunosuppression than each mAb by itself.

L4 ANSWER 28 OF 42 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN

AN 1992-03218 BIOTECHDS

TI A chimeric mouse/human anti-IL-2 receptor antibody with enhanced biological activities;
production of chimeric antibody against human p55 interleukin-2 receptor

AU Rose B; Gillespie A; Wunderlich D; Barbosa J A; Cahill K; *Zerler B

CS Miles

LO Molecular Therapeutics, Miles Research Center, 400 Morgan Lane, W. Haven,

CT 06516, USA.

SO Mol.Immunol.; (1992) 29, 1, 131-44
CODEN: MOIMD5

DT Journal

LA English

AN 1992-03218 BIOTECHDS

AB A chimeric mouse-human monoclonal antibody
ART-65 against human p55 interleukin-2 (IL-2)
receptor was constructed from immunoglobulin genes isolated from
mouse hybridoma AHT107, which binds to a different epitope on p55 than
IL-2 and does not inhibit proliferation of T-lymphocytes in mitogen and
mixed lymphocyte reaction peripheral blood mononuclear cell (PBMC)
stimulation assays. The chimeric antibodies (CAs) were made by joining
cDNA sequences corresponding to the variable regions of the light and
heavy chains of AHT107 to DNA encoding the human kappa light chain and
IgG-1 heavy chain constant regions, respectively. They were expressed in
CHO cells. The CAs had more anti-proliferative activity than their mouse
IgG-1 counterparts. The human constant region of the CAs interacted more
efficiently than the mouse constant region with effector components
present in the PBMC cultures. F(ab')₂ generated from the CAs did not
efficiently inhibit proliferation in the PBMC assays, and the chimeric
antibodies did not inhibit proliferation of an antigen specific, IL-2
dependent T-cell clone stimulated in the absence of PBMC. (50 ref)

L4 ANSWER 29 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1992:126503 CAPLUS

DN 116:126503

TI Monoclonal antibodies to common epitopes of the human α/β
T-cell receptor preferentially activate CD45RA⁺T-cells

AU Schwinzer, Reinhard; Schlitt, Hans Juergen; Wonigeit, Kurt

CS Klin. Abdom.-Transplantationschir., Med. Hochsch. Hannover, Hannover,
D-3000/61, Germany

SO Cellular Immunology (1992), 140(1), 31-41
CODEN: CLIMB8; ISSN: 0008-8749

DT Journal

LA English

AB The murine monoclonal antibody BMA 031 (IgG2b) is directed to a
monomorphic epitope on the human α/β T-cell receptor. In
contrast to anti-CD3 antibodies of the IgG2b isotype, BMA 031 is able to
induce a proliferative response in T-cells from IgG2b low responders.
This response occurs independently of crosslinking conditions indicating
that the mode of activation differs from stimulation by the anti-CD3
antibody OKT3 (IgG2a) which strictly depends on crosslinking conditions.
To further characterize the stimulatory potential of the two antibodies
the authors studied the lymphocyte subsets responsive to stimulation by
BMA 031 and OKT3. In CD45RA⁺ cells both antibodies exhibited similar
effects. They induced weak expression of the 55-kDa chain of the
interleukin-2 receptor (CD25), virtually no interleukin-2
secretion, but nevertheless strong proliferation. In CD45RO⁺ cells OKT3
and BMA 031 showed markedly different effects. OKT3 stimulated strong
CD25 expression, strong interleukin-2 production, and marked
proliferation. In contrast, CD45RO⁺ cells stimulated by BMA 031 showed
only weak CD25 expression but neither interleukin-2 production nor
proliferation. These data suggest that CD45RA⁺ and CD45RO⁺ cells differ
in their capability to produce interleukin-2 upon stimulation via the
CD3/T-cell receptor complex and also in the requirement for interleukin-2
to mount a proliferative response. The differential effect of OKT3 and
BMA 041 in CD435RO⁺ cells probably results from the failure of BMA 031 to
trigger interleukin-2 production which may be a consequence of its inability
to induce CD3/T-cell receptor crosslinking in IgG2b low responders. BMA
031 is therefore a useful tool for the selective activation of CD45RA⁺
cells in these individuals.

L4 ANSWER 30 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1991:677524 CAPLUS
 DN 115:277524
 TI Monoclonal antibodies defining distinct epitopes of the human IL-2 receptor β chain and their differential effects on IL-2 responses
 AU Ohbo, Kazuyuki; Takeshita, Toshikazu; Asao, Hironobu; Kurahayashi, Yumiyo; Tada, Kotaro; Mori, Hisashi; Hatakeyama, Masanori; Taniguchi, Tadatsugu; Sugamura, Kazuo
 CS Sch. Med., Tohoku Univ., Sendai, 980, Japan
 SO Journal of Immunological Methods (1991), 142(1), 61-72
 CODEN: JIMMBG; ISSN: 0022-1759
 DT Journal
 LA English
 AB Five new monoclonal antibodies (mAbs) were prepared which specifically immunoppt. the human interleukin-2 receptor β chain (IL-2R β). One of them, TU30, recognizes the intracytoplasmic serine-rich region of IL-2R β that is critical for IL-2 signal transduction. The others, TU12, TU21, TU23, and TU25, completely inhibit IL-2 binding, as does the previously characterized TU27. However, reciprocal binding competition assays show that the epitopes recognized by the individual mAbs are different from each other. The mAbs inhibit the growth of IL-2-dependent cells. The magnitude of their inhibitory effects is dependent on not only the affinities of the mAbs for IL-2R β but also upon the number of IL-2R α subunits expressed on IL-2-dependent cells. These mAbs should be useful in studying the structure and function of the IL-2R.

L4 ANSWER 31 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 1990:476262 CAPLUS
 DN 113:76262
 TI Characterization of OKT3-initiated lymphokine-activated effectors expanded with interleukin 2 and tumor necrosis factor α
 AU Yang, Stephen C.; Owen-Schaub, Laurie B.; Roth, Jack A.; Grimm, Elizabeth A.
 CS M. D. Anderson Cancer Cent., Univ. Texas, Houston, TX, 77030, USA
 SO Cancer Research (1990), 50(12), 3526-32
 CODEN: CNREA8; ISSN: 0008-5472
 DT Journal
 LA English
 AB Synergistic and cooperative effects in vivo of a monoclonal antibody to the CD3 T-cell determinant (OKT3), interleukin 2 (IL-2), and tumor necrosis factor α (TNF) as stimuli in generating effectors with lymphokine-activated killer activity were studied. Activation of human peripheral blood mononuclear cells with OKT3 (10 ng/mL) for 48 h, followed by culture in low concns. of IL-2 (10 units/mL) and TNF (250 units/mL) resulted in higher cell recovery (50- to 3300-fold) compared to the number of cells in the initial culture and enhanced lytic activity against both Raji and fresh tumor targets (mean 1900-fold) by day 30 compared to those expanded with higher concns. of IL-2 (100 unit/mL) alone. Immunofluorescence anal. of peripheral blood mononuclear cells initiated with OKT3 and expanded with IL-2 plus TNF revealed a selective increase in CD8+ cells and a decrease in CD4+ by day 28; the opposite effect was observed when cells were incubated with 100 units/mL of IL-2 alone, resulting in a greater proportion of CD4+ cells. Almost all cells were CD3+. Studies of cytokine receptor expression indicated that OKT3 plus IL-2 plus TNF caused an earlier up-regulation of the IL-2-receptor β chain (Tac) and higher TNF receptor expression by day 6 compared to 100 units/mL IL-2 alone. Significant TNF levels (>17 units/mL) were measured in culture supernatants from peripheral blood mononuclear cells initiated with OKT3 alone. Collectively, the data demonstrate that induction of lymphokine-activated killer activity with OKT3, followed by culture in low concentration of IL-2 plus TNF is an alternative to the use of high-dose IL-2 alone and suggest that this combination may provide potential advantages in long-term generation of cytolytic cells.

L4 ANSWER 32 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 1990:404529 CAPLUS
 DN 113:4529
 TI Monoclonal antibody to human interleukin 2 receptors and its use
 IN Wijdenes, John; Herve, Patrick; Clement, Claude; Morel-Fourrier, Brigitte;
 Peters, Andre
 PA Centre Regional de Transfusion Sanguine, Fr.
 SO Eur. Pat. Appl., 13 pp.
 CODEN: EPXXDW
 DT Patent
 LA German
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 340604	A2	19891108	EP 1989-107438	19890425
	EP 340604	A3	19900509		
	EP 340604	B1	19940302		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	DE 3815472	A1	19891116	DE 1988-3815472	19880506
	US 5084391	A	19920128	US 1989-343091	19890425
	AT 102253	E	19940315	AT 1989-107438	19890425
	ES 2061769	T3	19941216	ES 1989-107438	19890425
	CA 1340350	A1	19990126	CA 1989-598779	19890505
	JP 02013371	A2	19900117	JP 1989-114006	19890506
PRAI	DE 1988-3815472	A	19880506		
	EP 1989-107438	A	19890425		

AB A mouse IgG1 monoclonal antibody binds to an epitope of the human interleukin 2 (IL-2) receptor different from Tac, inhibits the binding of human IL-2 to its receptor, and is useful for treatment, prophylaxis, and diagnosis of IL-2-dependent diseases in humans. The antibody interacts with the 55- and 75-kilodalton subunits of the IL-2 receptor. Thus, mice were immunized with phytohemagglutinin-stimulated peripheral blood T-lymphocytes, their spleen cells were fused with mouse myeloma cells, and the hybridomas were cloned and screened for production of antibodies to activated T-cells. Monoclonal antibody B.B.10 and its Fab fragment inhibited the IL-2-induced proliferation of activated T-cells, inhibited the mixed lymphocyte reaction, and inhibited bone marrow transplant rejection and graft-vs.-host reaction in patients.

L4 ANSWER 33 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 1988:185117 CAPLUS
 DN 108:185117
 TI Preparation of pharmaceutical formulation comprising T-lymphocyte-specific suppressor monoclonal antibodies and their use in serotherapy
 IN Cobbold, Stephen Paul; Clark, Michael Ronald; Benjamin, Richard John;
 Waldmann, Herman
 PA Wellcome Foundation Ltd., UK
 SO Eur. Pat. Appl., 12 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 240344	A2	19871007	EP 1987-302864	19870402
	EP 240344	A3	19890816		
	EP 240344	B1	19931118		
	R: BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	JP 63002934	A2	19880107	JP 1987-82202	19870402
	JP 2562141	B2	19961211		
	EP 536807	A1	19930414	EP 1992-118716	19870402
	R: BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				

PRAI GB 1986-8068 A 19860402

AB Specific monoclonal antibodies directed against antigens on T-lymphocytes of a mammal (e.g. the CD4 and CD25 antigens) are capable of eliciting immune tolerance in a subject exposed to an antigen. Tolerogenic antibodies may be given at the same time or shortly after the presentation of an antigen, usually for a limited period of time. Tolerogenic vaccines may be prepared which can be applied in serotherapy of e.g. autoimmune diseases. Male CBA/Ca mice received mismatched skin grafts from BALB/c mice, together with monoclonal antibody injection 3 times per wk for 4 wk. The antibodies, anti-Lyt-2 (CD8), anti-L3T4 (CD4), and anti-IL-2 (CD25), were used either individually or in combination. None of the antibodies alone was sufficient to generate graft tolerance (though CD4 was the most effective). Combination of two monoclonal antibodies gave a much improved graft survival. Only the combination of all monoclonal antibodies (i.e. CD4, CD8, and CD25) allowed survival of the mismatched skin grafts indefinitely without further treatment. Thus tolerance induction by a monoclonal antibody sometimes requires the addition of particular other monoclonal antibodies, e.g. in the prevention of graft rejection. A combined pharmaceutical formulation consists of a tolerogenic antibody (e.g. anti-CD4) and therapeutic antibody (e.g. anti-CD8) dissolved in a solution containing 0.2M NaCl, 20 mM L-histidine, 1% weight/volume sorbitol, and 1% weight/volume human serum albumin. The preparation is sterile and free of pyrogen and abnormal toxicity. The formulation is subjected to freeze-drying.

L4 ANSWER 34 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1986:531919 CAPLUS

DN 105:131919

TI High- and low-affinity interleukin 2 receptors: distinctive effects of monoclonal antibodies

AU Fujii, Masahiro; Sugamura, Kazuo; Nakai, Shinichi; Tanaka, Yuetsu; Tozawa, Hideki; Hinuma, Yorio

CS Inst. Virus Res., Kyoto Univ., Kyoto, 606, Japan

SO Journal of Immunology (1986), 137(5), 1552-6

CODEN: JOIMA3; ISSN: 0022-1767

DT Journal

LA English

AB The effects of monoclonal antibodies to human interleukin 2 (IL 2) receptor on the binding of 125I-labeled IL 2 to high- and low-affinity receptors were examined by Scatchard plot anal. Two of these monoclonal antibodies, HIEI and H-47, reduced the IL 2-binding affinity of high-affinity receptors from a dissociation constant Kd of 14-20 pM to a Kd of 110-140 pM, but slightly raised that of low-affinity receptors. These 2 antibodies scarcely affected the nos. of high- and low-affinity receptors. On the other hand, H-31 completely blocked IL 2 binding to both high- and low-affinity receptors, and H-A26 slightly reduced the affinities of both high- and low-affinity receptors, from 17 pM to 28 pM and from 28 nM to 54 nM, resp. H-48 had little effect on IL 2 binding to high- or low-affinity receptors. By use of these monoclonal antibodies, the inhibitory effect of IL 2 on growth of a human T-lymphotropic virus type-immortalized T cell line was demonstrated to be transmitted from high-affinity, but not low-affinity, receptors.

L4 ANSWER 35 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1986:125797 CAPLUS

DN 104:125797

TI Bismuth-212-labeled anti-Tac monoclonal antibody: α -particle-emitting radionuclides as modalities for radioimmunotherapy

AU Kozak, Robert W.; Atcher, Robert W.; Gansow, Otto A.; Friedman, Arnold M.; Hines, John J.; Waldmann, Thomas A.

CS Inorg. Radioimmune Chem. Sect., Natl. Cancer Inst., Bethesda, MD, 20892, USA

SO Proceedings of the National Academy of Sciences of the United States of America (1986), 83(2), 474-8
CODEN: PNASA6; ISSN: 0027-8424

DT Journal

LA English

AB Anti-Tac, a monoclonal antibody directed to the human interleukin 2 (IL-2) receptor, has been successfully conjugated to the α -particle-emitting radionuclide ^{212}Bi by use of a bifunctional ligand, the isobutylcarboxycarbonic anhydride of DTPA. The phys. properties of ^{212}Bi are appropriate for radioimmunotherapy in that it has a short half-life, deposits its high energy over a short distance, and can be obtained in large quantities from a Ra generator. Antibody-specific activities of 1-40 $\mu\text{Ci}/\mu\text{g}$ were achieved. Specificity of the ^{212}Bi -labeled anti-Tac was demonstrated for the IL-2 receptor-pos. adult T-cell leukemia line HUT-102B2 by protein synthesis inhibition and clonogenic assays. Activity levels of 0.5 μCi or the equivalent of 12 rad/mL of α -radiation targeted by anti-Tac eliminated >98% the proliferative capabilities of HUT-102B2 cells with more modest effects on IL-2 receptor-neg. cell lines. Specific cytotoxicity was blocked by excess unlabeled anti-Tac but not by human IgG. In addition, an irrelevant control monoclonal antibody of the same isotype labeled with ^{212}Bi was unable to target α -radiation to cell lines. Therefore, ^{212}Bi -labeled anti-Tac is a potentially effective and specific immunocytotoxic reagent for the elimination of IL-2 receptor-pos. cells. These expts. thus provide the scientific basis for use of α -particle-emitting radionuclides in immunotherapy.

L4 ANSWER 36 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1986:404692 CAPLUS
DN 105:4692

TI Use of OKT3 and anti-TAC monoclonal antibodies for the quantitative evaluation of interleukin 2

AU Cornaglia-Ferraris, P.; Baffico, M.

CS Lab. Oncol. Pediatr., Ist. G. Gaslini, Genoa, 16148, Italy

SO Bollettino dell'Istituto Sieroterapico Milanese (1986), 64(6), 471-4
CODEN: BISMAL; ISSN: 0021-2547

DT Journal

LA Italian

AB A simple and rapid method is proposed for the qual. and quant. evaluation of interleukin 2 (IL-2). The method is based on the capacity of the monoclonal antibody OKT3 to induce the synthesis of IL-2 receptors on peripheral T lymphocytes and the capacity of the anti-TAC monoclonal antibody to block the binding of the IL-2 to its receptor, thereby inhibiting the T cell proliferation.

L4 ANSWER 37 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1985:518012 CAPLUS
DN 103:118012

TI Pseudomonas exotoxin conjugate immunotoxins

IN Pastan, I.; Willingham, M. C.; Fitzgerald, D. J.

PA United States Dept. of Health and Human Services, USA

SO U. S. Pat. Appl., 25 pp. Avail. NTIS Order No. PAT-APPL-6-574 173.
CODEN: XAXXAV

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	US 574173	A0	19850301	US 1984-574173	19840126
	US 4545985	A	19851008		
PRAI	US 1984-574173		19840126		

AB A new class of immunotoxins employing a monoclonal antibody, recognizing a

specific human cell receptor, bonded to Pseudomonas toxin, is presented. Pseudomonas Exotoxin is modified with Me 4-mercaptobutyrimidate [64821-63-2] so that, by itself, the toxin exhibits very little toxicity; coupling the modified toxin to a monoclonal antibody, however, transforms the toxin into a highly potent immunotoxin. For example, immunotoxin conjugates for Pseudomonas exotoxin coupled to anti-TFR (antibody to the transferrin receptor) and anti-TAC (antibody to the human T-cell growth factor receptor) and to epidermal growth factor [62229-50-9] are disclosed.

L4 ANSWER 38 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1985:130190 CAPLUS

DN 102:130190

TI Functional properties of the 50 kd protein associated with the E-receptor on human T lymphocytes: suppression of IL 2 production by anti-p50 monoclonal antibodies

AU Tadmori, Waleed; Reed, John C.; Nowell, Peter C.; Kamoun, Malek

CS Dep. Pathol., Univ. Pennsylvania, Philadelphia, PA, 19104, USA

SO Journal of Immunology (1985), 134(3), 1709-16

CODEN: JOIMA3; ISSN: 0022-1767

DT Journal

LA English

AB Monoclonal antibody 9.6 is specific for a 50 kd T cell surface protein (p50) associated with the sheep erythrocyte (E)-receptor on human T lymphocytes. This antibody interferes with many T cell functions. The effect of antibody 9.6 on lymphocyte proliferation and interleukin 2 (IL 2) production triggered by mitogens, soluble antigens, and alloantigens was examined to elucidate the mechanism(s) of its immunosuppressive action. At concns. as low as 50 ng/mL, 9.6 suppressed lymphocyte proliferation and the elaboration of IL 2 by T cells stimulated by phytohemagglutinin (PHA), alloantigens, or low concns. of the phorbol ester TPA (≤ 1 ng/mL). Furthermore, in cultures stimulated by a combination of PHA plus TPA, 9.6 did not inhibit the acquisition of IL 2 receptors but inhibited proliferation and IL 2 production. Immunoaffinity-purified IL 2 completely restored lymphocyte proliferation in cultures inhibited by 9.6. Studies of kinetics of inhibition by 9.6 showed that this antibody inhibited lymphocyte proliferation induced by PHA, alloantigen, and purified protein derivative of tuberculin even when added at 24, 48, and 72 h, resp., after the initiation of these cultures, suggesting that 9.6 does not block lectin binding or antigen recognition by T cells and that it can inhibit lymphocyte proliferation even after cells have undergone one or more rounds of cell division. A dose-response anal. of lymphocyte proliferation induced by PHA or by TPA demonstrated that the degree of inhibition by 9.6 decreased with increasing concns. of these mitogens. Antibody 9.6 did not inhibit lymphocyte response induced by optimal concns. of PHA (50 to 100 μ g/mL; PHA-M) but inhibited proliferation of maximally induced lymphocytes by using a synergistic combination of low concns. of PHA (5 μ g/mL, PHA-M) plus TPA (1 ng/mL). These findings indicate that 1) 9.6 inhibits lymphocyte proliferation by affecting IL 2 production, 2) 9.6 does not inhibit the acquisition of 9.6 receptors induced by a synergistic combination of PHA plus TPA, and 3) p50 mols. may be involved in multiple pathways of T cell activation.

L4 ANSWER 39 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1984:470760 CAPLUS

DN 101:70760

TI Human T lymphocyte activation by monoclonal antibodies; OKT3, but not UCHT1, triggers mitogenesis via an interleukin 2-dependent mechanism

AU Van Wauwe, Jean P.; Goossens, Jan G.; Beverley, Peter C. L.

CS Dep. Immunochem., Janssen Pharm. Res. Lab., Beerse, B-2340, Belg.

SO Journal of Immunology (1984), 133(1), 129-32

CODEN: JOIMA3; ISSN: 0022-1767

DT Journal

LA English

AB OKT3 and UCHT1 monoclonal antibodies, which recognize the same human T cell surface antigen, induce proliferation in T lymphocytes. The mechanism by which these antibodies trigger DNA synthesis in human peripheral blood mononuclear cell (PBMC) cultures was compared. Whereas PBMC from all donors tested were mitogenically inducible by OKT3, cells from only 25 of 40 donors were responsive to UCHT1. UCHT1 treatment of PBMC from responders, but not from nonresponders, resulted in the expression by T cells of membrane binding sites reactive with anti-Tac monoclonal antibody, which specifies the human interleukin 2 (IL 2) receptor. UCHT1-induced PBMC supernatants from nonresponders, but unexpectedly, also from responders, contained no measurable IL 2 activity. Anti-Tac monoclonal antibody failed to suppress UCHT1-triggered [3H]thymidine incorporation into PBMC from responsive donors. By contrast, OKT3 treatment of PBMC from all donors led to the emergence of IL 2 receptors, and substantial IL 2 production, and the resultant DNA synthesis was inhibitable by anti-Tac antibody. These data indicate that the interaction of OKT3 and UCHT1 monoclonal antibodies with the same T cell structure leads to the induction of proliferation via 2 different mechanisms: 1 dependent on the availability of IL 2 (OKT3) and 1 independent on the production and processing of this lymphokine (UCHT1). PBMC unresponsiveness to UCHT1 could therefore not be related to a dysfunction in IL 2 synthesis or IL 2 receptor display.

L4 ANSWER 40 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1983:556561 CAPLUS

DN 99:156561

TI Production and characterization of monoclonal antibodies to human interleukin 2: strategy and tactics

AU Smith, Kendall A.; Favata, Margaret F.; Oroszlan, Stephen

CS Dep. Med., Dartmouth Med. Sch., Hanover, NH, 03756, USA

SO Journal of Immunology (1983), 131(4), 1808-15

CODEN: JOIMA3; ISSN: 0022-1767

DT Journal

LA English

AB The unique hormonal characteristics of human interleukin 2 (IL 2), primarily the high affinity of the IL 2-receptor interaction, created several impediments to the generation of monoclonal antibodies to this lymphokine. Because normal cell sources produce only a few micrograms of IL 2 per L, it was necessary to utilize high producer clones and subclones of a human T leukemia cell line (JURKAT) to obtain immunogenic amts. of IL 2 protein. Moreover, assays that required antibody-mediated intervention of the high affinity IL 2-receptor binding were ineffectual in the identification of anti-IL 2-producing hybridomas, thus necessitating the development of immunoassays. Two of 3 initially derived antibodies detected by enzyme-linked immunoassay reacted specifically with IL 2 as demonstrated by antibody concentration-dependent neutralization of IL 2 activity.

The neutralization of cellular proliferation was specific for IL 2-reactive cells, coincided with an inhibition of IL 2 receptor binding, could be completely overcome by affinity-purified IL 2 and was species-specific; human and murine IL 2 were neutralized, whereas rat IL 2 activity remained unaffected. A 3rd antibody, although much less effective in neutralizing IL 2 activity, bound to IL 2 more avidly and functioned as an efficient immunoabsorbent. IL 2 could be concentrated and purified by immunoabsorption from crude conditioned medium in a single step. The purified product, which retained biol. activity, was made up of a single protein (mol. weight = 15,500) as determined by SDS-polyacrylamide gel electrophoresis, reversed-phase liquid chromatog., and N-terminal amino acid sequence anal.

L4 ANSWER 41 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1983:486331 CAPLUS

DN 99:86331
 TI Blockade of the interleukin-2 receptor by anti-Tac antibody:
 inhibition of human lymphocyte activation
 AU Depper, Joel M.; Leonard, Warren J.; Robb, Richard J.; Waldmann, Thomas
 A.; Greene, Warner C.
 CS Metab. Branch, Natl. Cancer Inst., Bethesda, MD, 20205, USA
 SO Journal of Immunology (1983), 131(2), 690-6
 CODEN: JOIMA3; ISSN: 0022-1767
 DT Journal
 LA English
 AB It was previously shown that monoclonal anti-Tac antibody (anti-Tac) inhibits the proliferation of interleukin-2 (IL-2)-dependent human continuous T cell lines. Further, it was shown that anti-Tac specifically blocks >95% of the binding of radiolabeled IL-2 to a continuous T cell line. It was suggested that anti-Tac antibody may bind to and block the human T cell receptor for IL-2. The effects of anti-Tac on the activation of human peripheral blood T lymphocytes were studied. Anti-Tac: 1) blocks T cell proliferation induced by soluble antigens (80-90%), autologous antigens (90%), and alloantigens (75-90%), 2) partially inhibits T cell proliferation induced by mitogenic lectins, including Con A (50-88%), pokeweed mitogen (40-87%), and phytohemagglutinin (20-80%); 3) abrogates (>95%) the generation of cytolytic T lymphocytes in allogeneic cell cocultures, but does not inhibit killing by cytolytic T lymphocytes once formed; and 4) inhibits T cell-dependent pokeweed mitogen activated B cell Ig production (78-95%). Anti-Tac inhibition of proliferation is not secondary to diminished production of IL-2. Finally, in antigen-induced T cell proliferative assays, the addition of highly purified IL-2 reverses the inhibitory effects of anti-Tac. Apparently, anti-Tac recognizes the human IL-2 receptor; this antibody can be used to modulate the human immune response.

L4 ANSWER 42 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 1984:4419 CAPLUS
 DN 100:4419
 TI Monoclonal anti-Tac blocks the action and membrane binding of
 human interleukin-2
 AU Depper, Joel M.; Leonard, Warren J.; Smith, Kendall A.; Waldmann, Thomas
 A.; Greene, Warner C.
 CS Metab. Branch, Natl. Cancer Inst., Bethesda, MD, USA
 SO Interleukins, Lymphokines, Cytokines, Proc. Int. Lymphokine Workshop, 3rd
 (1983), Meeting Date 1982, 19-26. Editor(s): Oppenheim, Joost J.; Cohen,
 Stanley; Landy, Maurice. Publisher: Academic, New York, N. Y.
 CODEN: 500PAC
 DT Conference; General Review
 LA English
 AB A review with 14 refs. of the authors' ongoing research discussing
 evidence that a monoclonal antibody originally defined as blocking T-cell
 activation (Tac) is actually directed to the
 interleukin-2-receptor.

12/9/10 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0006880984 BIOSIS NO.: 199038058875
IL-2 RECEPTOR-DIRECTED IMMUNOTHERAPY A MODEL OF IMMUNE INTERVENTION
BOOK TITLE: MELCHERS, F. (ED.). PROGRESS IN IMMUNOLOGY, VOL. VII; 7TH
INTERNATIONAL CONGRESS OF IMMUNOLOGY, BERLIN, WEST GERMANY, 1989.
CI+1318P. SPRINGER-VERLAG NEW YORK, INC.: SECAUCUS, NEW JERSEY, USA;
BERLIN, WEST GERMANY. ILLUS
AUTHOR: WALDMANN T A (Reprint); GOLDMAN C K; BAMFORD R; BURTON J; JUNGHANS
R
AUTHOR ADDRESS: METABOLISM BRANCH, NATL CANCER INST, NATL INST HEALTH,
BETHESDA, MD 20892, USA**USA
p1201-1212 1989
ISBN: 0-387-51053-2; 3-540-51053-2
DOCUMENT TYPE: Book; Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH
DESCRIPTORS: REVIEW HUMAN MONOCLONAL ANTIBODY ANTI-TAC IMMUNOLOGIC-DRUG
ANTINEOPLASTIC-DRUG INTERLEUKIN-2 LEUKEMIA LYMPHOMA
DESCRIPTORS:
MAJOR CONCEPTS: Clinical Endocrinology--Human Medicine, Medical Sciences;
Endocrine System--Chemical Coordination and Homeostasis; Oncology--
Human Medicine, Medical Sciences; Pharmacology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata,
Animalia
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates;
Vertebrates
CONCEPT CODES:
00520 General biology - Symposia, transactions and proceedings
10064 Biochemistry studies - Proteins, peptides and amino acids
12512 Pathology - Therapy
17002 Endocrine - General
22005 Pharmacology - Clinical pharmacology
22016 Pharmacology - Endocrine
22018 Pharmacology - Immunological processes and allergy
24008 Neoplasms - Therapeutic agents and therapy
24010 Neoplasms - Blood and reticuloendothelial neoplasms
34508 Immunology - Immunopathology, tissue immunology
BIOSYSTEMATIC CODES:
86215 Hominidae

12/9/11 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0006674475 BIOSIS NO.: 198987122366
PROLIFERATION OF HIGHLY PURIFIED T CELLS IN RESPONSE TO SIGNALING VIA
SURFACE RECEPTORS REQUIRES CELL-CELL CONTACT
AUTHOR: SCHWARTZ D (Reprint); WONG R C K; CHATILA T; ARNAOUT A; MILLER R;
GEHA R
AUTHOR ADDRESS: CHILD HOSP, DIV IMMUNOL, 300 LONGWOOD AVE, BOSTON, MASS
02115, USA**USA
JOURNAL: Journal of Clinical Immunology 9 (2): p151-158 1989
ISSN: 0271-9142
DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: Lymphocyte proliferation is associated with cell-cell aggregation. In order to assess the importance of cell-cell contact in T-cell proliferation we examined the effect of disruption of cellular aggregation by anti LFA-14 mAb on T-cell proliferation. Monocyte-dependent T-cell proliferation induced by anti-CD3 mAb, pairs of anti-CD2 mAbs, or PHA was inhibited by anti-LFA-1 mAb. Monocyte-independent proliferation of highly purified T cells to anti-CD3 mAb plus PMA or plus IL-2 and to PHA plus IL-2 was, surprisingly, also inhibited by anti-LFA-1 mAb. Anti-LFA-1 mAb caused the partial inhibition of both low-affinity and high-affinity IL-2 receptor and the complete inhibition of IL-2 synthesis. In contrast to the above, the proliferation of highly purified T cells to PMA plus ionomycin was not inhibited by anti-LFA-1 mAb. These results suggest that optimal activation of highly purified T cells via cell surface receptors requires LFA-1-dependent cell-to-cell contact between proliferating T cells as well as between T cells and accessory cells. Such contact appears to be crucial for initiating IL-2 production and for optimal action of IL-2 through its receptors.

DESCRIPTORS: HUMAN MONOCLONAL ANTIBODY LYMPHOCYTE FUNCTION-ASSOCIATED ANTIGEN INTERLEUKIN 2

DESCRIPTORS:

MAJOR CONCEPTS: Blood and Lymphatics--Transport and Circulation; Cell Biology; Development; Endocrine System--Chemical Coordination and Homeostasis; Membranes--Cell Biology

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

CONCEPT CODES:

02508 Cytology - Human
10064 Biochemistry studies - Proteins, peptides and amino acids
10508 Biophysics - Membrane phenomena
15004 Blood - Blood cell studies
15008 Blood - Lymphatic tissue and reticuloendothelial system
17002 Endocrine - General
25508 Development and Embryology - Morphogenesis
34502 Immunology - General and methods

BIOSYSTEMATIC CODES:

86215 Hominidae

12/9/12 (Item 10 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0006183288 BIOSIS NO.: 198886023209

RECOMBINANT INTERLEUKIN 2 AND ANTI-TAC INFLUENCE THE GROWTH OF ENRICHED MULTIPOTENT HEMOPOIETIC PROGENITORS PROPOSED HYPOTHESES FOR DIFFERENT RESPONSES IN EARLY AND LATE PROGENITORS

AUTHOR: MICHALEVIC R (Reprint); CAMPANA D; KATZ F E; JANOSSY G; HOFFBRAND A V

AUTHOR ADDRESS: INST HEMATOLOGY, ICHILOV HOSP, TEL-AVIV 64239, ISRAEL**
ISRAEL

JOURNAL: Leukemia Research 12 (2): p113-122 1988

ISSN: 0145-2126

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: Experiments were designed to evaluate the effect of recombinant IL-2 on growth of hemopoietic precursors from different sources (normal cord blood and bone marrow, and PB from CGL patients). For this purpose, combined cell sorting techniques and multipotent colony forming cell assays were used. A monoclonal antibody BI-4C5, which recognizes an antigen present on early lympho-myeloid cells as well as on all colony forming cells (CFU-GEMM assay), was used to enrich the studied populations. Double colour immunofluorescence techniques were performed to analyse the expression of Tac antigen on early progenitors. The results showed that rIL-2 had a stimulatory effect on growth of enriched progenitors from the three sources and surprisingly that addition of anti-Tac did not abolish this effect. On the contrary, anti-Tac enhanced even more growth of these sorted BI-3C5 precursors, suggesting a ligand action of the antibody. More interestingly, a low percentage of cord cells (1 in 1000) expressed both BI-3C5 and Tac antigens. The vast majority of cells did not concomitantly express both markers. The double labelled cells had a lymphoid-like morphology, high nucleus/cytoplasmic ratio and 2-3 nucleoli. The results will be discussed focusing on early and late "stem" cell growth.

DESCRIPTORS: HUMAN MONOCLONAL ANTIBODY NEOPLASTIC B-CELL PROGENITORS**DESCRIPTORS:**

MAJOR CONCEPTS: Blood and Lymphatics--Transport and Circulation; Cell Biology; Development

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

CONCEPT CODES:

02508 Cytology - Human

10064 Biochemistry studies - Proteins, peptides and amino acids

10068 Biochemistry studies - Carbohydrates

15004 Blood - Blood cell studies

15006 Blood - Blood, lymphatic and reticuloendothelial pathologies

15008 Blood - Lymphatic tissue and reticuloendothelial system

24010 Neoplasms - Blood and reticuloendothelial neoplasms

25508 Development and Embryology - Morphogenesis

BIOSYSTEMATIC CODES:

86215 Hominidae

12/9/13 (Item 11 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0006155124 BIOSIS NO.: 198885124015

ACTIVATION AND DIFFERENTIATION ANTIGEN EXPRESSION IN B-CELL NON-HODGKIN'S LYMPHOMA

AUTHOR: SALTER D M (Reprint); KRAJEWSKI A S; CUNNINGHAM S

AUTHOR ADDRESS: UNIV MED SCH, EDINBURGH EH8 9AG, UK**UK

JOURNAL: Journal of Pathology 154 (3): p209-222 1988

ISSN: 0022-3417

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: In an attempt to establish whether extended immuno-phenotyping

allows more accurate definition of subgroups of B-cell non-Hodgkin's lymphoma (NHL) we have stained a series of 145 cases with a large panel of monoclonal antibodies that recognize B-cell differentiation and activation antigens. No antigen was expressed by all cases. The B-cell histogenesis in many cases could be confirmed only by using a panel of immunoglobulin and pan B-cell markers. There was marked phenotypic heterogeneity within and between major groups of B-cell NHL as delineated by the Kiel classification although the differentiation antigens CD5 (lymphocytic and centrocytic NHL) and OKT10 (plasma cell tumors) were more often expressed by certain morphological groups. The activation antigens 4F2 and transferrin receptor were expressed more strongly and more often by high grade NHL but other activation antigens (CD23 and CD25) were not more frequently associated with these tumors. Extended phenotyping may be of value in improving the understanding of biological abnormalities and processes involved in B-cell NHL, but we conclude that a limited panel of markers (CD3, CD5, CD22, CD45, IgM, kappa, and lambda) should be sufficient for routine diagnosis and classification of most cases.

DESCRIPTORS: HUMAN MONOCLONAL ANTIBODY HISTOGENESIS TRANSFERRIN DIAGNOSIS
DESCRIPTORS:

MAJOR CONCEPTS: Blood and Lymphatics--Transport and Circulation; Clinical Endocrinology--Human Medicine, Medical Sciences; Hematology--Human Medicine, Medical Sciences; Metabolism; Oncology--Human Medicine, Medical Sciences; Pathology

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

CONCEPT CODES:

10064 Biochemistry studies - Proteins, peptides and amino acids
10068 Biochemistry studies - Carbohydrates
10069 Biochemistry studies - Minerals
12504 Pathology - Diagnostic
13004 Metabolism - Carbohydrates
13012 Metabolism - Proteins, peptides and amino acids
15006 Blood - Blood, lymphatic and reticuloendothelial pathologies
15008 Blood - Lymphatic tissue and reticuloendothelial system
24001 Neoplasms - Diagnostic methods
24003 Neoplasms - Immunology
24010 Neoplasms - Blood and reticuloendothelial neoplasms
34502 Immunology - General and methods
34508 Immunology - Immunopathology, tissue immunology

BIOSYSTEMATIC CODES:

86215 Hominidae

12/9/14 (Item 12 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0006110480 BIOSIS NO.: 198885079371

**NOVEL INTERLEUKIN 2 IL-2 RECEPTOR APPEARS TO MEDIATE IL-2-INDUCED
ACTIVATION OF NATURAL KILLER CELLS**

AUTHOR: KEHRI J H (Reprint); DUKOVICH M; WHALEN G; KATZ P; FAUCI A S;
GREENE W C

AUTHOR ADDRESS: NIH, BLDG 10, RM 11B-13, BETHESDA, MD 20892, USA**USA

JOURNAL: Journal of Clinical Investigation 81 (1): p200-205 1988

ISSN: 0021-9738

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: A novel IL-2 receptor, distinct from the Tac protein, has been identified on the surface of purified human natural killer (NK) cells by chemical cross-linking of 125I-IL-2. This protein is .apprx.70,000 D in size (p70) and appears to be identical to the recently recognized second subunit of the human high affinity IL-2 receptor complex. Scatchard analysis of 125I-IL-2 binding to purified NK cells revealed .apprx. 2,300 p70 binding sites per cell with an apparent dissociation constant of 200 pM, a value intermediate between the previously recognized high and low affinity forms of the human IL-2 receptor. The monoclonal anti-Tac antibody did not inhibit the cross-linking of 125I-IL-2 to the p70 binding sites present on NK cells. Functionally, the addition of high concentrations of recombinant IL-2 to the enriched NK cells promoted a rapid augmentation of cytolytic activity and a more delayed increase in cellular proliferation. Anti-Tac effectively blocked the IL-2-induced proliferative response in these cells, but failed to alter the enhancement of cytotoxicity. Analysis of NK cytoplasmic RNA isolated at various time points after IL-2 stimulation revealed the rapid induction of c-myc and Tac gene expression that was also not inhibited by the anti-Tac antibody. These findings suggest that IL-2 binding to the p70 receptor constitutively expressed on the surface of NK cells may mediate both the development of increased cytolytic activity and rapid changes in gene expression. The activation of the Tac gene may in turn permit the formation of the high affinity IL-2 receptor complex (comprised of at least the Tac and p70 proteins) that appears to transduce the requisite signals involved in NK cell proliferation.

DESCRIPTORS: HUMAN MONOCLONAL ANTIBODY GENE EXPRESSION

DESCRIPTORS:

MAJOR CONCEPTS: Blood and Lymphatics--Transport and Circulation; Cell Biology; Clinical Endocrinology--Human Medicine, Medical Sciences; Development; Genetics; Metabolism

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

CONCEPT CODES:

02508 Cytology - Human

03508 Genetics - Human

06504 Radiation biology - Radiation and isotope techniques

10059 Biochemistry methods - Minerals

10064 Biochemistry studies - Proteins, peptides and amino acids

10068 Biochemistry studies - Carbohydrates

13012 Metabolism - Proteins, peptides and amino acids

15008 Blood - Lymphatic tissue and reticuloendothelial system

25508 Development and Embryology - Morphogenesis

34502 Immunology - General and methods

34508 Immunology - Immunopathology, tissue immunology

BIOSYSTEMATIC CODES:

86215 Hominidae

12/9/15 (Item 13 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0006100711 BIOSIS NO.: 198885069602

REMARKABLE DEPRESSION OF CD4-POSITIVE 2H4-POSITIVE T CELLS IN SEVERE

CHRONIC ACTIVE EPSTEIN-BARR VIRUS INFECTION

AUTHOR: FRANCO E (Reprint); KAWA-HA K; DOI S; YUMURA K; MURATA M; ISHIHARA S; TAWA A; YABUUCHI H

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JOURNAL: Scandinavian Journal of Immunology 26 (6): p769-774 1987

ISSN: 0300-9475

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: In order to better understand the features of chronic active Epstein-Barr (EB) virus infection, we employed two-color immunofluorescence staining with monoclonal antibodies and flow cytometry analysis to study the lymphocyte phenotypes of two patients with severe symptoms of this disorder as well as four patients with mild symptoms. We found an increased number of activated T cells, as characterized by CD4+Ia+, CD8+Ia+, or CD4+Tac+ phenotypes, and a markedly decreased CD4+2H4+ T cell subpopulation, previously characterized as a suppressor-induced subset, in the patients with severe symptoms. In contrast, the four patients with mild symptoms showed only a slightly elevated number of activated T cells and a normal CD4+2H4+/CD4+ ratio. These phenotypic differences may suggest heterogeneity in this disorder. Also, a failure in the suppressor-inducer population could contribute to changes in the host-virus relationship and the degree of the decrease in this population may correlate directly with the severity of the disease.

DESCRIPTORS: HUMAN MONOCLONAL ANTIBODY IMMUNOFLUORESCENCE

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Blood and Lymphatics--Transport and Circulation; Clinical Endocrinology--Human Medicine, Medical Sciences; Hematology--Human Medicine, Medical Sciences; Infection

BIOSYSTEMATIC NAMES: Herpesviridae--dsDNA Viruses, Viruses, Microorganisms; Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

COMMON TAXONOMIC TERMS: Double-Stranded DNA Viruses; Microorganisms; Viruses; Animals; Chordates; Humans; Mammals; Primates; Vertebrates

CONCEPT CODES:

02508 Cytology - Human
06504 Radiation biology - Radiation and isotope techniques
10064 Biochemistry studies - Proteins, peptides and amino acids
10068 Biochemistry studies - Carbohydrates
15004 Blood - Blood cell studies
15006 Blood - Blood, lymphatic and reticuloendothelial pathologies
15008 Blood - Lymphatic tissue and reticuloendothelial system
34502 Immunology - General and methods
34508 Immunology - Immunopathology, tissue immunology
36006 Medical and clinical microbiology - Virology

BIOSYSTEMATIC CODES:

03115 Herpesviridae
86215 Hominidae

12/9/16 (Item 14 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0005265469 BIOSIS NO.: 198682111856

ELEVATED TITERS OF CELL-FREE INTERLEUKIN 2 RECEPTOR IN SERUM AND

CEREBROSPINAL FLUID SPECIMENS OF PATIENTS WITH ACQUIRED IMMUNODEFICIENCY SYNDROME

AUTHOR: SETHI K K (Reprint); NAEHER H

AUTHOR ADDRESS: INST MED MICROBIOL IMMUNOL, UNIV BONN, 5300 BONN, VENUSBERG

JOURNAL: Immunology Letters 13 (4): p179-184 1986

ISSN: 0165-2478

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: A sensitive monoclonal antibody based ELISA was used to detect cell-free interleukin-2 receptor (IL-2R) in the body fluids of patients with acquired immune deficiency syndrome (AIDS), a variety of other disease conditions and a control group of apparently healthy (heterosexual and homosexual) males. Two of the 25 control donors showed low titers (1:8) of IL-2 receptor in the serum samples; the cerebrospinal fluid (CSF) specimens from these individuals proved negative. However, serum and CSF specimens from all the 9 patients with AIDS showed significantly elevated titers (range 1:128 to 1:4096) of IL-2 receptor. The presence of moderate titers (range 1:128 to 1:512) of circulating IL-2 receptor could also be detected in all of the 4 patients with acute lymphocytic leukemia. IL-2 receptor was detectable in the CSF and/or serum specimens from 3 of 3 patients with lung cancer, 3 of 4 patients with acute hepatitis B infection, and 2 of 3 patients with multiple sclerosis. IL-2 receptor could not be detected in the serum or CSF specimens originating from patients with legionellosis (3/3), asthma (3/3), or those with nonpulmonary febrile bacterial infections (4/4). It is concluded that soluble IL-2 receptor may be found in serum or CSF specimens from patients with certain (but not all) disease conditions including AIDS. The conspicuously elevated titers of cell-free IL-2R in the body fluids of patients with AIDS may contribute to the drastic impairment of the immune system regulation observed in such patients.

DESCRIPTORS: HUMAN MONOCLONAL ANTIBODY ACUTE LYMPHOCYTIC LEUKEMIA LUNG CANCER ACUTE HEPATITIS B MULTIPLE SCLEROSIS

DESCRIPTORS:

MAJOR CONCEPTS: Clinical Endocrinology--Human Medicine, Medical Sciences; Gastroenterology--Human Medicine, Medical Sciences; Immune System--Chemical Coordination and Homeostasis; Infection; Microbiology; Neurology--Human Medicine, Medical Sciences; Oncology--Human Medicine, Medical Sciences; Physiology; Pulmonary Medicine--Human Medicine, Medical Sciences

BIOSYSTEMATIC NAMES: Viruses--Microorganisms; Retroviridae--DNA and RNA Reverse Transcribing Viruses, Viruses, Microorganisms; Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

COMMON TAXONOMIC TERMS: DNA and RNA Reverse Transcribing Viruses; Microorganisms; Viruses; Animals; Chordates; Humans; Mammals; Primates; Vertebrates

CONCEPT CODES:

10064 Biochemistry studies - Proteins, peptides and amino acids
10508 Biophysics - Membrane phenomena
12504 Pathology - Diagnostic
14006 Digestive system - Pathology
15006 Blood - Blood, lymphatic and reticuloendothelial pathologies
15008 Blood - Lymphatic tissue and reticuloendothelial system
15010 Blood - Other body fluids
16006 Respiratory system - Pathology
20506 Nervous system - Pathology
24004 Neoplasms - Pathology, clinical aspects and systemic effects
24010 Neoplasms - Blood and reticuloendothelial neoplasms

33506 Virology - Animal host viruses
34504 Immunology - Bacterial, viral and fungal
34508 Immunology - Immunopathology, tissue immunology
36006 Medical and clinical microbiology - Virology

BIOSYSTEMATIC CODES:

03000 Viruses
03305 Retroviridae
86215 Hominidae

12/9/17 (Item 15 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0005130055 BIOSIS NO.: 198681093946

**EXPRESSION OF INTERLEUKIN 2 RECEPTOR ON T CELL CHRONIC LYMPHOCYTIC LEUKEMIA
CELLS AND THEIR RESPONSE TO INTERLEUKIN 2**

AUTHOR: TSUDO M (Reprint); UCHIYAMA T; UMADOME H; WANO Y; HORI T; TAMORI S;
UCHINO H; KITA K; CHIBA S; ET AL

AUTHOR ADDRESS: FIRST DIV INTERNAL MED, FAC MED, KYOTO UNIV, 54
SHOGGIN-KAWARAMACHI, SAKYO-KU, KYOTO 606, JPN**JAPAN

JOURNAL: Blood 67 (2): p316-321 1986

ISSN: 0006-4971

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: We analyzed peripheral blood leukemic cells from six patients with T cell chronic lymphocytic leukemia (T-CLL) with monoclonal antibodies including the anti-Tac antibody, which recognizes the receptor for interleukin 2 (IL 2). The patients were divided into two groups according to the reactivity of the monoclonal antibodies. Leukemic cells from three patients with T-CLL reacted with OKT3 and T4 but not T8, whereas those from the remaining three patients reacted with OKT3 and T8 but not T4. IL2 receptor, which is expressed on activated T cells but not on resting T cells, was preferentially expressed on T4+ T-CLL cells. The IL 2 receptor on T4+ T-CLL cells was indistinguishable from that on normal activated T cells with respect to molecular weight and downregulation by the anti-Tac antibody. Moreover, fresh T4+ T-CLL cells, but not T8+ T-CLL cells, proliferated in response to exogenous IL 2 without prior activation, and this proliferation was inhibited by the anti-Tac antibody. These results suggest that malignant growth of T4+ T-CLL cells can be regulated by IL 2 not only in vitro but also in vivo.

DESCRIPTORS: HUMAN MONOCLONAL ANTIBODY

DESCRIPTORS:

MAJOR CONCEPTS: Blood and Lymphatics--Transport and Circulation; Clinical Endocrinology--Human Medicine, Medical Sciences; Hematology--Human

Medicine, Medical Sciences; Oncology--Human Medicine, Medical Sciences
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

CONCEPT CODES:

10064 Biochemistry studies - Proteins, peptides and amino acids
10068 Biochemistry studies - Carbohydrates
12504 Pathology - Diagnostic
15006 Blood - Blood, lymphatic and reticuloendothelial pathologies
15008 Blood - Lymphatic tissue and reticuloendothelial system
24003 Neoplasms - Immunology

24010 Neoplasms - Blood and reticuloendothelial neoplasms
34508 Immunology - Immunopathology, tissue immunology
BIOSYSTEMATIC CODES:
86215 Hominidae

12/9/18 (Item 16 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0004994859 BIOSIS NO.: 198631075758
PHENOTYPIC ALTERATION OF LEUKEMIC HAIRY CELLS UPON INTERFERON-ALPHA
TREATMENT IN-VITRO
AUTHOR: GASTL G (Reprint); AULITZKY W; MARTH C; TILG H; LEITER E;
GATTRINGER C; HUBER C
AUTHOR ADDRESS: UNIVERSITAETSKLINIK F INNERE MEDIZIN, A-6020 INNSBRUCK**
AUSTRIA
JOURNAL: Journal of Cancer Research and Clinical Oncology 111 (SUPPL): p
S40 1986
CONFERENCE/MEETING: 18TH NATIONAL CANCER CONGRESS OF THE GERMAN CANCER
SOCIETY, MUNICH, WEST GERMANY, MAR. 4-8, 1986. J CANCER RES CLIN ONCOL.
ISSN: 0171-5216
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH
DESCRIPTORS: ABSTRACT HUMAN MONOCLONAL ANTIBODY FMC-7 MONOCLONAL ANTIBODY
LEW-M-5 MONOCLONAL ANTIBODY LYT 3 MONOCLONAL ANTIBODY BMA-030 MONOCLONAL
ANTIBODY ANTI-TAC ANTINEOPLASTIC-DRUG IMMUNOLOGIC-DRUG
DESCRIPTORS:
MAJOR CONCEPTS: Blood and Lymphatics--Transport and Circulation;
Endocrine System--Chemical Coordination and Homeostasis; Immune System
--Chemical Coordination and Homeostasis; Oncology--Human Medicine,
Medical Sciences; Pharmacology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata,
Animalia
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates;
Vertebrates
CONCEPT CODES:
00520 General biology - Symposia, transactions and proceedings
02508 Cytology - Human
10064 Biochemistry studies - Proteins, peptides and amino acids
10068 Biochemistry studies - Carbohydrates
10508 Biophysics - Membrane phenomena
12512 Pathology - Therapy
15008 Blood - Lymphatic tissue and reticuloendothelial system
17002 Endocrine - General
22005 Pharmacology - Clinical pharmacology
22016 Pharmacology - Endocrine
22018 Pharmacology - Immunological processes and allergy
24003 Neoplasms - Immunology
24008 Neoplasms - Therapeutic agents and therapy
24010 Neoplasms - Blood and reticuloendothelial neoplasms
34502 Immunology - General and methods
BIOSYSTEMATIC CODES:
86215 Hominidae

12/9/19 (Item 17 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0004649473 BIOSIS NO.: 198579068372

INTERLEUKIN 2 REGULATES THE EXPRESSION OF TAC ANTIGEN ON PERIPHERAL BLOOD T LYMPHOCYTES

AUTHOR: WELTE K (Reprint); ANDREEFF M; PLATZER E; HOLLOWAY K; RUBIN B Y;
MOORE M A S; MERTELSMANN R

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**USA

JOURNAL: Journal of Experimental Medicine 160 (5): p1390-1403 1984

ISSN: 0022-1007

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: The effect of OKT3 antibody and interleukin 2 (IL-2) on Tac antigen expression and the proliferation of human peripheral blood mononuclear leukocytes was investigated. OKT3 monoclonal antibody at low, nonmitogenic concentrations (25 pg/ml) or IL-2 alone at optimal concentrations (20 U/ml) did not induce IL-2 receptor expression, as measured by Tac antibody or by T cell proliferation. Costimulation with these concentrations of OKT3 antibody and IL-2 led to Tac antigen expression and T cell proliferation. The data suggest that the T cells are activated in 2 steps: OKT3 antibody at 25 pg/ml does not induce Tac antigen expression, but preactivates T cells to become responsive to IL-2. The addition of exogenous IL-2 then leads to expression of the IL-2 receptor, as recognized by Tac antibody, and to subsequent proliferation.

DESCRIPTORS: HUMAN MONOCLONAL ANTIBODY OKT-3

DESCRIPTORS:

MAJOR CONCEPTS: Blood and Lymphatics--Transport and Circulation; Cell Biology; Clinical Endocrinology--Human Medicine, Medical Sciences; Immune System--Chemical Coordination and Homeostasis; Metabolism

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

CONCEPT CODES:

02508 Cytology - Human

10064 Biochemistry studies - Proteins, peptides and amino acids

10068 Biochemistry studies - Carbohydrates

10506 Biophysics - Molecular properties and macromolecules

10508 Biophysics - Membrane phenomena

13012 Metabolism - Proteins, peptides and amino acids

15008 Blood - Lymphatic tissue and reticuloendothelial system

17002 Endocrine - General

34502 Immunology - General and methods

34508 Immunology - Immunopathology, tissue immunology

BIOSYSTEMATIC CODES:

86215 Hominidae

12/9/20 (Item 1 from file: 73)

DIALOG(R)File 73:EMBASE

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11717940 EMBASE No: 2002290941

Monoclonal antibodies in the treatment of psoriasis

ANTICUERPOS MONOCLONALES EN EL TRATAMIENTO DE LA PSORIASIS

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Actas Dermo-Sifiliograficas (ACTAS DERM-SIFILIOGR.) (Spain) 2002,
93/6 (355-367)
CODEN: ADSIA ISSN: 0001-7310
DOCUMENT TYPE: Journal ; Review
LANGUAGE: SPANISH SUMMARY LANGUAGE: ENGLISH; SPANISH
NUMBER OF REFERENCES: 34

One of the mechanisms used to interfere in the physiopathologic processes involved in the development of diseases and achieve clinical improvement in patients is the application of monoclonal antibodies. Their development has been associated with severe side effects until chimeric and humanized antibodies appeared. Ligands of receptors and immunoconjugates with toxins have also been used to interfere in these processes. Although many molecules have been developed against the targets implied in psoriasis only some have shown positive results in clinical trials. Some of them are close to approval for their use in psoriasis: Xanelim(R) (efalizumab, anti-CD11a) and Amevive(R) (alefacept, anti-CD2). Other drugs are approved for other indications and could gain approval in psoriasis such as Remicade(R) (infliximab, anti-TNF-alpha) Enbrel(R) (etanercept, antiTNF-alpha) and Zenapax(R) (daclizumab, anti-CD25). In the following years, these drugs will change our approach to the treatment of psoriasis, using intravenous infusions or intramuscular or subcutaneous injections at weekly or biweekly intervals, with scanty side effects.

BRAND NAME/MANUFACTURER NAME: xanelim; amevive; remicade; enbrel; zenapax; nuvion; humax t4; primatized

DRUG DESCRIPTORS:

*monoclonal antibody--adverse drug reaction--ae; *monoclonal antibody--clinical trial--ct; *monoclonal antibody--drug dose--do; *monoclonal antibody--drug therapy--dt; *monoclonal antibody--intramuscular drug administration--im; *monoclonal antibody--intravenous drug administration--iv; *monoclonal antibody--subcutaneous drug administration--sc; *alefacept--adverse drug reaction--ae; *alefacept--clinical trial--ct; *alefacept--drug dose--do; *alefacept--drug therapy--dt; *alefacept--intramuscular drug administration--im; *alefacept--intravenous drug administration--iv; *alefacept--subcutaneous drug administration--sc; *infliximab--adverse drug reaction--ae; *infliximab--clinical trial--ct; *infliximab--drug dose--do; *infliximab--drug therapy--dt; *infliximab--intramuscular drug administration--im; *infliximab--intravenous drug administration--iv; *infliximab--subcutaneous drug administration--sc; *etanercept--adverse drug reaction--ae; *etanercept--clinical trial--ct; *etanercept--drug dose--do; *etanercept--drug therapy--dt; *etanercept--intramuscular drug administration--im; *etanercept--intravenous drug administration--iv; *etanercept--subcutaneous drug administration--sc; *interleukin 2 receptor antibody--adverse drug reaction--ae; *interleukin 2 receptor antibody--clinical trial--ct; *interleukin 2 receptor antibody--drug dose--do; *interleukin 2 receptor antibody--drug therapy--dt; *interleukin 2 receptor antibody--intramuscular drug administration--im; *interleukin 2 receptor antibody--intravenous drug administration--iv; *interleukin 2 receptor antibody--subcutaneous drug administration--sc; chimeric antibody--adverse drug reaction--ae; chimeric antibody--clinical trial--ct; chimeric antibody--drug dose--do; chimeric antibody--drug therapy--dt; chimeric antibody--intramuscular drug administration--im; chimeric antibody--intravenous drug administration--iv; chimeric antibody--subcutaneous drug administration--sc; human monoclonal antibody--adverse drug reaction--ae; human monoclonal antibody--clinical trial--ct; human monoclonal antibody--drug dose--do; human monoclonal antibody--drug therapy--dt; human monoclonal antibody--intramuscular drug administration--im;

human monoclonal antibody--intravenous drug administration--iv; human monoclonal antibody--subcutaneous drug administration--sc; monoclonal antibody CD3--adverse drug reaction--ae; monoclonal antibody CD3--clinical trial--ct; monoclonal antibody CD3--drug dose--do; monoclonal antibody CD3--drug therapy--dt; monoclonal antibody CD3--intramuscular drug administration--im; monoclonal antibody CD3--intravenous drug administration--iv; monoclonal antibody CD3--subcutaneous drug administration--sc; OKT 4--adverse drug reaction--ae; OKT 4--clinical trial--ct; OKT 4--drug dose--do; OKT 4--drug therapy--dt; OKT 4--intramuscular drug administration--im; OKT 4--intravenous drug administration--iv; OKT 4--subcutaneous drug administration--sc; CD40 ligand monoclonal antibody--adverse drug reaction--ae; CD40 ligand monoclonal antibody--clinical trial--ct; CD40 ligand monoclonal antibody--drug dose--do; CD40 ligand monoclonal antibody--drug therapy--dt; CD40 ligand monoclonal antibody--intramuscular drug administration--im; CD40 ligand monoclonal antibody--intravenous drug administration--iv; CD40 ligand monoclonal antibody--subcutaneous drug administration--sc; intercellular adhesion molecule 3--adverse drug reaction--ae; intercellular adhesion molecule 3--clinical trial--ct; intercellular adhesion molecule 3--drug dose--do; intercellular adhesion molecule 3--drug therapy--dt; intercellular adhesion molecule 3--intramuscular drug administration--im; intercellular adhesion molecule 3--intravenous drug administration--iv; intercellular adhesion molecule 3--subcutaneous drug administration--sc; interleukin 8--adverse drug reaction--ae; interleukin 8--clinical trial--ct; interleukin 8--drug dose--do; interleukin 8--drug therapy--dt; interleukin 8--intramuscular drug administration--im; interleukin 8--intravenous drug administration--iv; interleukin 8--subcutaneous drug administration--sc; visilizumab--adverse drug reaction--ae; visilizumab--clinical trial--ct; visilizumab--drug dose--do; visilizumab--drug therapy--dt; visilizumab--intramuscular drug administration--im; visilizumab--intravenous drug administration--iv; visilizumab--subcutaneous drug administration--sc; OKT 3--adverse drug reaction--ae; OKT 3--clinical trial--ct; OKT 3--drug dose--do; OKT 3--drug therapy--dt; OKT 3--intramuscular drug administration--im; OKT 3--intravenous drug administration--iv; OKT 3--subcutaneous drug administration--sc; receptor; ligand; antibody conjugate; toxin; unclassified drug

MEDICAL DESCRIPTORS:

*psoriasis--drug therapy--dt
side effect--side effect--si; drug approval; drug indication; drug effect; dose response; drug activity; human; clinical trial; review
DRUG TERMS (UNCONTROLLED): efalizumab--adverse drug reaction--ae; efalizumab--clinical trial--ct; efalizumab--drug dose--do; efalizumab--drug therapy--dt; efalizumab--intramuscular drug administration--im; efalizumab--intravenous drug administration--iv; efalizumab--subcutaneous drug administration--sc; monoclonal antibody CD2--adverse drug reaction--ae; monoclonal antibody CD2--clinical trial--ct; monoclonal antibody CD2--drug dose--do; monoclonal antibody CD2--drug therapy--dt; monoclonal antibody CD2--intramuscular drug administration--im; monoclonal antibody CD2--intravenous drug administration--iv; monoclonal antibody CD2--subcutaneous drug administration--sc; monoclonal antibody cd6--adverse drug reaction--ae; monoclonal antibody cd6--clinical trial--ct; monoclonal antibody cd6--drug dose--do; monoclonal antibody cd6--drug therapy--dt; monoclonal antibody cd6--intramuscular drug administration--im; monoclonal antibody cd6--intravenous drug administration--iv; monoclonal antibody cd6--subcutaneous drug administration--sc; monoclonal antibody cd11a--adverse drug reaction--ae; monoclonal antibody cd11a--clinical trial--ct; monoclonal antibody cd11a--drug dose--do; monoclonal antibody cd11a--drug therapy--dt; monoclonal antibody cd11a--intramuscular drug administration--im; monoclonal antibody cd11a--intravenous drug administration--iv; monoclonal antibody cd11a--subcutaneous drug administration--sc; monoclonal

antibody cd25--adverse drug reaction--ae; monoclonal antibody cd25
 --clinical trial--ct; monoclonal antibody cd25--drug dose--do; monoclonal
 antibody cd25--drug therapy--dt; monoclonal antibody cd25--intramuscular
 drug administration--im; monoclonal antibody cd25--intravenous drug
 administration--iv; monoclonal antibody cd25--subcutaneous drug
 administration--sc; monoclonal antibody CD80--adverse drug reaction--ae;
 monoclonal antibody CD80--clinical trial--ct; monoclonal antibody CD80
 --drug dose--do; monoclonal antibody CD80--drug therapy--dt; monoclonal
 antibody CD80--intramuscular drug administration--im; monoclonal antibody
 CD80--intravenous drug administration--iv; monoclonal antibody CD80
 --subcutaneous drug administration--sc; monoclonal antibody CD86--adverse
 drug reaction--ae; monoclonal antibody CD86--clinical trial--ct; monoclonal
 antibody CD86--drug dose--do; monoclonal antibody CD86--drug therapy--dt;
 monoclonal antibody CD86--intramuscular drug administration--im; monoclonal
 antibody CD86--intravenous drug administration--iv; monoclonal antibody
 CD86--subcutaneous drug administration--sc; humax t4; primatized
 CAS REGISTRY NO.: 214745-43-4 (efalizumab); 222535-22-0 (alefacept);
 170277-31-3 (infliximab); 185243-69-0, 200013-86-1 (etanercept);
 179045-86-4 (interleukin 2 receptor antibody); 114308-91-7 (interleukin
 8); 219716-33-3 (visilizumab); 140608-64-6 (OKT 3)

SECTION HEADINGS:

- 013 Dermatology and Venereology
- 037 Drug Literature Index
- 038 Adverse Reaction Titles

12/9/21 (Item 2 from file: 73)

DIALOG(R)File 73:EMBASE

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10913817 EMBASE No: 2000410486

**Lipopolysaccharide-dependent induction of leech leukocytes that
 cross-react with vertebrate cellular differentiation markers**

De Equileor M.; Grimaldi A.; Tettamanti G.; Valvassori R.; Cooper E.L.;
 Lanzavecchia G.

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 Varese Italy

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Tissue and Cell (TISSUE CELL) (United Kingdom) 2000, 32/5 (437-445)

CODEN: TICEB ISSN: 0040-8166

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 35

We have designed experiments to characterise leech leukocytes that
 mediates inflammatory responses. Shortly after inflicting injury to the
 body wall in the presence of lipopolysaccharides, many cells resembling
 macrophages, NK cells and granulocytes of vertebrates and many
 invertebrates migrated to the lesioned area. Nuclei of migrating cells
 incorporated bromodeoxyuridine. Using human monoclonal antibodies,
 macrophage-like cells were positive for CD25, CD14, CD61, CD68, CD11b and
 CD11c. NK-like cells were positive for CD25, CD56, CD57 and CD16, and
 granulocytes were positive for CD11b and CD11c. In blots of leech extracts,
 the CD25 monoclonal antibody recognised a band of about 55 kD; the CD56
 monoclonal antibody, two bands of about 140 and 210 kD; the CD57 monoclonal
 antibody, two bands of about 106 and 70 kD; the CD14 monoclonal antibody, a
 band of about 50 kD; the CD16 monoclonal antibody, a band of about 60 kD.
 CD61 and CD68 both recognised a band of about 110 kD; CD11b recognised a
 band of 200 kD, and CD11c, a band of 180 kD. (C) 2000 Harcourt Publishers
 Ltd.

DRUG DESCRIPTORS:

*Escherichia coli lipopolysaccharide; *leukocyte antigen--endogenous compound--ec; *biological marker--endogenous compound--ec
human monoclonal antibody--endogenous compound--ec; interleukin 2 receptor
--endogenous compound--ec; CD14 antigen--endogenous compound--ec;
glycoprotein p 15095--endogenous compound--ec; CD68 antigen--endogenous
compound--ec; CD11b antigen--endogenous compound--ec; CD56 antigen
--endogenous compound--ec; CD57 antigen--endogenous compound--ec; CD16
antigen--endogenous compound--ec; unclassified drug

MEDICAL DESCRIPTORS:

*leukocyte
controlled study; nonhuman; animal cell; leech; vertebrate; inflammation;
macrophage activation; natural killer cell; granulocyte; cell migration;
cell adhesion; immune system; cell differentiation; cross reaction; immune
response; antigen recognition; article

DRUG TERMS (UNCONTROLLED): cd61 antigen--endogenous compound--ec

SECTION HEADINGS:

- 026 Immunology, Serology and Transplantation
- 029 Clinical and Experimental Biochemistry

12/9/22 (Item 1 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

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11880166 Genuine Article#: 705MQ Number of References: 28

**Title: Treatment of graft-versus-host disease after liver transplantation
with basiliximab followed by bowel resection**

Author(s): Sudhindran S; Taylor A; Delriviere L; Collins VP; Liu L; Taylor
CJ; Alexander GJ; Gimson AE; Jamieson NV; Watson CJE; Gibbs P
(REPRINT)

Corporate Source: Addenbrookes NHS Trust, Dept Transplantat, Cambridge CB2
2QQ//England/ (REPRINT); Addenbrookes NHS Trust, Dept
Transplantat, Cambridge CB2 2QQ//England/; Addenbrookes NHS Trust, Dept
Histopathol, Cambridge CB2 2QQ//England/; Addenbrookes NHS Trust, Dept
Tissue Typing, Cambridge CB2 2QQ//England/

Journal: AMERICAN JOURNAL OF TRANSPLANTATION, 2003, V3, N8 (AUG), P
1024-1029

ISSN: 1600-6135 Publication date: 20030800

Publisher: BLACKWELL MUNKSGAARD, 35 NORRE SOGADE, PO BOX 2148, DK-1016
COPENHAGEN, DENMARK

Language: English Document Type: ARTICLE

Geographic Location: England

Journal Subject Category: SURGERY; TRANSPLANTATION

Abstract: Graft-versus-host disease (GVHD) after orthotopic liver
transplantation (OLT) is a serious complication with mortality rates
over 80%. Two patients with established GVHD after OLT were treated
with Basiliximab, a chimeric murine human monoclonal antibody which
binds to the alpha-chain of interleukin-2 receptor (IL-214). Two males,
aged 45 and 56 years, presented after OLT with a clinical picture
consistent with GVHD. Quantitative measurements of recipient peripheral
blood donor lymphocyte chimerism were carried out by flow cytometric
analysis, and showed peak chimerism levels of 5% and 8%, respectively.
Treatment comprised 3 doses of 1 g methyl prednisolone followed by 2
doses of 20mg of Basiliximab. In both, treatment resulted in complete
disappearance of macro-chimerism in blood. There was resolution of skin
rash by day 7; however, diarrhea persisted. White cell scan showed
increased uptake in the terminal ileum and small-bowel resection was
performed in both patients. One patient is alive and well 36 months

after OLT. The other patient had resolution of GVHD, but died of recurrent hepatitis C 1 year after OLT. The combination of immunological and surgical treatment for GVHD following solid organ transplantation has not previously been described.

Descriptors--Author Keywords: basiliximab ; GVHD ; liver transplant

Identifiers--KeyWord Plus(R): PRIMERS PCR-SSP; IL-2/IL-2 RECEPTOR SYSTEM; HEPATITIS-C; RECIPIENT; ANTIBODY; AMPLIFICATION; RECURRENCE; THERAPY

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03026784 Genuine Article#: MX920 Number of References: 37

Title: HUMANIZATION OF MOUSE ANTI-HUMAN IL-2 RECEPTOR ANTIBODY B-B10

Author(s): NAKATANI T; LONE YC; YAMAKAWA J; KANAOKA M; GOMI H; WIJDENES J; NOGUCHI H

Corporate Source: SUMITOMO PHARMACEUT CO LTD,DISCOVERY RES LABS 2,RES CTR,KONOHANA KU,1-98 KASUGADE NAKA 3/OSAKA 554//JAPAN/; SUMITOMO CHEM CO LTD,TAKARAZUKA RES CTR,BIOTECHNOL LAB/TAKARAZUKA/HYOGO 665/JAPAN/; CTR REG TRANSFUS SANGUINE/F-25020 BESANCON//FRANCE/

Journal: PROTEIN ENGINEERING, 1994, V7, N3 (MAR), P435-443

ISSN: 0269-2139

Language: ENGLISH Document Type: ARTICLE

Geographic Location: JAPAN; FRANCE

Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences

Journal Subject Category: BIOCHEMISTRY & MOLECULAR BIOLOGY

Abstract: Mouse monoclonal anti-human IL-2 receptor antibody (B-B10)

inhibits IL-2-dependent human T-cell proliferation. It has been used in clinical trials in the transplantation field and promising results are being accumulated. Mouse B-B10 antibody was humanized by grafting all

CDRs and some framework amino acid residues onto human antibodies, KAS for V-H and PAY for V-k. Nine humanized B-B10s with differently grafted framework residues were constructed and assessed for their biological activities. One of these humanized B-B10, M5, showed nearly the same activity as the mouse B-B10. The 49th residue of V-k was demonstrated to play a crucial role in the antigen-antibody interaction by 3-D structure analysis with a computer modeling system.

Descriptors--Author Keywords: CDR GRAFT ; COMPUTER MODELING ; HUMANIZED ANTIBODY ; SITE-DIRECTED MUTAGENESIS

Identifiers--KeyWords Plus: RESHAPING HUMAN-ANTIBODIES; HUMAN MONOCLONAL-ANTIBODY; HYPERVARIABLE REGIONS; HUMAN-IMMUNOGLOBULIN; IMMUNE-RESPONSE; THERAPY; EXPRESSION; GENES; RESOLUTION; SEGMENTS

Research Fronts: 92-0799 008 (ANTIBODY ENGINEERING; ANTIGEN COMBINING SITE; FILAMENTOUS PHAGE; PROTEIN TARGETS)

92-0078 002 (PROTEIN SECONDARY STRUCTURE; ARTIFICIAL NEURAL NETWORKS; ALPHA-HELIX PREDICTION)

92-8137 002 (MONOCLONAL-ANTIBODY CONJUGATE; MYELOMA CELL EXPRESSION; THERAPY OF HUMAN CERVICAL TUMOR XENOGRAFTS)

92-4812 001 (PUTATIVE ANAEROBIC COPROPORPHYRINOGEN-III OXIDASE IN RHODOBACTER-SPHAEROIDES; TRANSCRIPTIONAL REGULATORY ELEMENT; FUNCTIONAL EXPRESSION)

92-7774 001 (MESSENGER-RNA STABILITY IN ESCHERICHIA-COLI; TOBACCO ETCH VIRUS NIA PROTEINASE; CITRATE SYNTHASES; CATALYTIC DOMAIN; INHIBITION OF REPA SYNTHESIS)

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DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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02350631 Genuine Article#: KV637 Number of References: 23
Title: INVITRO SENSITIZATION FOR HUMAN MONOCLONAL-ANTIBODY PRODUCTION
Author(s): NIEDEBALA W; KURPISZ M
Corporate Source: POLISH ACAD SCI, INST HUMAN GENET, UL STRZESZYNSKA
32/PL-60479 POZNAN//POLAND/; POLISH ACAD SCI, INST HUMAN GENET, UL
STRZESZYNSKA 32/PL-60479 POZNAN//POLAND/; DEUTSCH RHEUMAFORSCH
ZENTRUM/BERLIN//GERMANY/

Journal: IMMUNOLOGY LETTERS, 1993, V35, N2 (FEB), P93-100
ISSN: 0165-2478

Language: ENGLISH Document Type: ARTICLE
Geographic Location: POLAND; GERMANY
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences
Journal Subject Category: IMMUNOLOGY

Abstract: We have found that cell adhesion prior to in vitro antigenic stimulation enriched the B-cell population and diminished the CD8 lymphocyte subset. These changes in lymphocyte proportions were favourable for increasing the percentage of antibody-producing cells after culturing in vitro followed by Epstein-Barr virus (EBV) infection. The immunodepletion of leukocytes by methyl esters did not yield satisfying results under analogous culture conditions. In vitro primary antigenic stimulations with the addition of IL-2 (25 U/ml medium) and low amounts of interferon-gamma provided better recruitment of antibody-producing cells and higher binding activity of antibodies to sperm than secondary antigenic stimulation. IL-6 did not positively influence the EBV-transformed cell lines.

Identifiers--KeyWords Plus: LEUCINE METHYL-ESTER; B-CELLS; LYMPHOCYTES; IMMUNIZATION

Research Fronts: 91-0808 001 (IL-2 RECEPTOR; HUMAN INTERLEUKIN-6; MURINE T-CELLS REQUIRES EXPRESSION)

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DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

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01736338 Genuine Article#: HX190 Number of References: 155

Title: HUMAN T-CELL LYMPHOTROPIC VIRUSES - REVIEW AND PROSPECTS FOR
ANTIVIRAL THERAPY

Author(s): PALKER TJ

Corporate Source: DUKE UNIV,MED CTR,POB 3307/DURHAM//NC/27710

Journal: ANTIVIRAL CHEMISTRY & CHEMOTHERAPY, 1992, V3, N3, P127-139

Language: ENGLISH Document Type: REVIEW

Geographic Location: USA

Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences

Journal Subject Category: BIOCHEMISTRY & MOLECULAR BIOLOGY; PHARMACOLOGY &
PHARMACY

Abstract: The human T-cell lymphotropic viruses types I and II (HTLV-I, II) pose challenges to researchers and clinicians who seek to unveil mechanisms of viral transformation and pathogenesis. HTLV-I infection in humans is associated with a wide array of primary and secondary diseases ranging from mild immunosuppression to adult T-cell leukaemia/lymphoma and HTLV-associated myelopathy/tropical spastic paraparesis (HAM/TSP), a neurological degenerative syndrome. As retroviruses, HTLV-I and II share similar replicative cycles with human immunodeficiency virus (HIV), the causative agent of acquired immunodeficiency syndrome. However, in contrast to HIV-I which destroys CD4+ T cells, HTLV-I and II can preferentially transform a CD4+ T-cell subset to an unrestricted growth state.

HTLV-I and II, along with simian T-lymphotropic virus (STLV) and bovine leukaemia virus (BLV), form a phylogenetic group which is distinct from ungulate, non-human primate and human lentiviruses such as visna, simian immunodeficiency virus (SIV), and human immunodeficiency viruses types 1 and 2. The proviral genome of HTLV-I is flanked at the 5' and 3' ends by long terminal repeats (LTR) and is further subdivided into structural gag and env genes, a pro gene encoding an aspartyl protease, a pol gene which encodes reverse transcriptase and endonuclease, and the regulatory gene elements tax and rex. Regions within the LTR contain recognition sites for cellular proteins and the tax gene product that collectively promote viral expression. Tax-mediated activation of cellular genes involved in growth and differentiation is suspected to play a dominant role in the leukaemogenic process associated with HTLV-I infection. Differential rex-regulated splicing of viral message gives rise to transcripts encoding the polyprotein precursor gag-pro-pol (unspliced), envelope (single spliced), or tax/rex (doubly spliced). The 100nm HTLV virion contains an electron-dense core surrounding a divalent-single stranded DNA genome. This core is in turn enclosed by concentric shells of matrix protein and an outer lipid bilayer, the latter acquired as the virus buds from the surface of the infected cell. Envelope glycoproteins associated with the outside of this lipid bilayer can interact with viral receptors on cells and mediate virus entry. Antiviral strategies have been directed at inhibiting viral entry into cells (sulphated and non-sulphated polysaccharides, vaccines), blocking of viral replication (AZT, suramin), intracellular immunization (transdominant repression of rex), and elimination of virus infected cells (IL-2 receptor-directed toxins). Serological screening of the blood supply and curtailing breast feeding of children by HTLV-I+

mothers have likely had a major impact in preventing HTLV-I infection.

Identifiers--KeyWords Plus: LONG TERMINAL REPEAT; TROPICAL SPASTIC PARAPARESIS; COMPLETE NUCLEOTIDE-SEQUENCE; HUMAN MONOCLONAL-ANTIBODY; LEUKEMIA-LYMPHOMA VIRUS; I-ASSOCIATED MYELOPATHY; CORD BLOOD CULTURES; TAX TRANSGENIC MICE; HTLV-I; MESSENGER-RNA

Research Fronts: 90-0323 008 (ANTI-HUMAN T-CELL LEUKEMIA-VIRUS TYPE-I ANTIBODY; TROPICAL SPASTIC PARAPARESIS; PERINATAL INFECTION)

90-0429 001 (NF-KAPPA-B TRANSCRIPTION FACTOR; DROSOPHILA HOMEODOMAIN PROTEINS; C-MYC GENE; EMBRYONIC EXPRESSION PATTERN; POU-SPECIFIC DOMAIN)

90-0596 001 (HUMAN-IMMUNODEFICIENCY-VIRUS TYPE-1; TAT PROTEIN; REV RESPONSE ELEMENT REGION)

90-1511 001 (HUMAN-IMMUNODEFICIENCY-VIRUS INFECTION; ANTIRETROVIRAL THERAPY IN AIDS; 2',3'-DIDEOXYINOSINE (DDI); HIV-1 REPLICATION INVITRO)

90-6267 001 (MURINE B-CELL LYMPHOMA; MONOCLONAL ANTIIDIDIOTYPIC ANTIBODIES; SHARED IDIOTYPE EXPRESSION; CHRONIC LYMPHOCYTIC-LEUKEMIA; BIOLOGICAL RESPONSE MODIFIERS)

90-6490 001 (MURINE ACQUIRED-IMMUNODEFICIENCY-SYNDROME; ZIDOVUDINE PROPHYLAXIS; ANTIRETROVIRAL THERAPY IN AIDS; INVIVO TOXICITY OF 3'-AZIDO-3'-DEOXYTHYMIDINE (AZT))

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YOSHIDA M, 1982, V79, P2031, P NATL ACAD SCI USA
YOSHIDA M, 1984, V81, P2534, P NATL ACAD SCI USA
ZAZOPOULOS E, 1990, V3, P1135, J ACQ IMM DEF SYND

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Set	Items	Description
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S1	12	SIMULECT AND (HUMAN (W) MONOCLONAL (W) ANTIBODY)
S2	12	RD S1 (unique items)
S3	305	DACLIZUMAB AND (TAC OR (IL (W) 2)) AND ANTIBODY
S4	0	S3 AND (HUMAN (W) MONOCLONAL)
S5	0	S3 AND (HUMAN (1W) ANTIBODY)
S6	210	S3 AND HUMAN
S7	3	S6 AND (IL (W) 2 (W) BINDING)
S8	3	RD S7 (unique items)
S9	6876	(HUMAN (W) MONOCLONAL (W) ANTIBODY)
S10	61840	(CD25 OR TAC OR (IL (W) 2 (W) RECEPTOR))
S11	27	S9 AND S10
S12	25	RD S11 (unique items)
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Logon file001 23aug06 12:48:41

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***EMCare (File 45)

***Trademarkscan - South Korea (File 655)

***Regulatory Affairs Journals (File 183)

***Index Chemicus (File 302)

***Inspec (File 202)

RESUMED UPDATING

***File 141, Reader's Guide Abstracts

RELOADS COMPLETED

***File 11, PsycInfo

***File 516, D&B--Dun's Market Identifiers

***File 523, D&B European Dun's Market Identifiers

***File 531, American Business Directory

*** The 2005 reload of the CLAIMS files (Files 340, 341, 942)

is now available online.

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***File 196, FINDEX ***File 468, Public Opinion Online (POLL)

Chemical Structure Searching now available in Prous Science Drug Data Report (F452), Prous Science Drugs of the Future (F453), IMS R&D Focus (F445/955), Pharmaprojects (F128/928), Beilstein Facts (F390), Derwent Chemistry Resource (F355) and Index Chemicus (File 302).

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File 1:ERIC 1966-2006/Jul

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Cost is in DialUnits

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B 155, 159, 10, 203, 35, 5, 467, 73, 434, 34

23aug06 12:49:15 User290558 Session D70.1

\$0.88 0.252 DialUnits File1

\$0.88 Estimated cost File1

\$0.14 INTERNET

\$1.02 Estimated cost this search

\$1.02 Estimated total session cost 0.252 DialUnits

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File 159:Cancerlit 1975-2002/Oct

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***File 159: Cancerlit is no longer updating.**

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File 73:EMBASE 1974-2006/Aug 23

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File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec

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File 34:SciSearch(R) Cited Ref Sci 1990-2006/Aug W2

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S SIMULECT AND (HUMAN (W) MONOCLONAL (W) ANTIBODY)

Processing

Processing

Processed 10 of 10 files ...

Completed processing all files

881 SIMULECT

17510383 HUMAN

850917 MONOCLONAL

1769948 ANTIBODY

6876 HUMAN(W) MONOCLONAL(W) ANTIBODY

S1 12 SIMULECT AND (HUMAN (W) MONOCLONAL (W) ANTIBODY)

?

?

RD S1

S2 12 RD S1 (unique items)

?

TYPE S2/FULL/1-12

2/9/1 (Item 1 from file: 73)

DIALOG(R)File 73:EMBASE

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13743302 EMBASE No: 2006144054

Antibody engineering for the development of therapeutic antibodies

Kim S.J.; Park Y.; Hong H.J.

H.J. Hong, Laboratory of Antibody Engineering, Korea Research Institute of Bioscience and Biotechnology, Daejeon 305-333 South Korea

AUTHOR EMAIL: hjhong@kribb.re.kr

Molecules and Cells (MOL. CELLS) (South Korea) 2005, 20/1 (17-29)

CODEN: MOCEE ISSN: 1016-8478

DOCUMENT TYPE: Journal ; Short Survey

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 100

Therapeutic antibodies represent one of the fastest growing areas of the pharmaceutical industry. There are currently 19 monoclonal antibodies in the market that have been approved by the FDA and over 150 in clinical developments. Driven by innovation and technological developments, therapeutic antibodies are the second largest biopharmaceutical product category after vaccines. Antibodies have been engineered by a variety of methods to suit a particular therapeutic use. This review describes the structural and functional characteristics of antibody and the antibody engineering for the generation and optimization of therapeutic antibodies. (c)KSCMB 2005.

BRAND NAME/MANUFACTURER NAME: OKT 3/Ortho; reopro/Centocor; panorex/Centocor; rituxan/Idex; zenapax/pdl; herceptin/Genentech; synagis/Medimmune; simulect/Novartis; remicade/Centocor; mylotarg/Celltech; campath/Millennium; zevalin/Idex; humira/cat; xolair/Tanox; raptiva/Xoma; bexxar/Corixa; erbitux/Imclone; avastin/Genentech

MANUFACTURER NAMES: Ortho; Centocor; Glaxo SmithKline; Idex; pdl; Genentech; Medimmune; Novartis; Celltech; Millennium; cat; BASF; Tanox; Xoma; Corixa; Imclone

DRUG DESCRIPTORS:

*monoclonal antibody--drug therapy--dt

human monoclonal antibody--drug therapy--dt; CD3 antibody--drug therapy--dt; abciximab--drug therapy--dt; edrecolomab--drug therapy--dt; rituximab--drug therapy--dt; daclizumab--drug therapy--dt; trastuzumab--drug therapy--dt; palivizumab--drug therapy--dt; basiliximab--drug therapy--dt; infliximab--drug therapy--dt; gentuzumab ozogamicin--drug therapy--dt; alemtuzumab--drug therapy--dt; ibritumomab tiuxetan--drug therapy--dt; adalimumab--drug therapy--dt; omalizumab--drug therapy--dt; efalizumab--drug therapy--dt; tositumomab--drug therapy--dt; cetuximab--drug therapy--dt; bevacizumab--drug therapy--dt; chimeric antibody; cell cycle protein; immunoglobulin G1 antibody--pharmacokinetics--pk; unclassified drug; OKT 3; tositumomab i 131

MEDICAL DESCRIPTORS:

antibody engineering; drug industry; food and drug administration; antibody structure; graft rejection--drug therapy--dt; transluminal coronary angioplasty; colorectal cancer--drug therapy--dt; nonhodgkin lymphoma--drug therapy--dt; kidney graft rejection--drug therapy--dt; kidney graft rejection--prevention--pc; metastasis--drug therapy--dt; breast cancer--drug therapy--dt; Respiratory syncytial pneumovirus; virus infection--drug therapy--dt; rheumatoid arthritis--drug therapy--dt; Crohn disease--drug therapy--dt; acute granulocytic leukemia--drug therapy--dt; B cell leukemia--drug therapy--dt; chronic lymphatic leukemia--drug therapy--dt; asthma--drug therapy--dt; psoriasis--drug therapy--dt; kidney cancer--drug therapy--dt; phage display; antibody library; antibody screening; transgenic mouse; immunogenicity; antigen binding; binding affinity; effector cell; antibody dependent cellular cytotoxicity; protein engineering; plasma half life; human; nonhuman; short survey

DRUG TERMS (UNCONTROLLED): muromanab--drug therapy--dt

CAS REGISTRY NO.: 143653-53-6 (abciximab); 174722-31-7 (rituximab);
 180288-69-1 (trastuzumab); 188039-54-5 (palivizumab); 170277-31-3 (
 infliximab); 216503-57-0 (alemtuzumab); 206181-63-7 (ibritumomab
 tiuxetan); 331731-18-1 (adalimumab); 242138-07-4 (omalizumab);
 214745-43-4 (efalizumab); 208921-02-2 (tositumomab); 205923-56-4 (
 cetuximab); 216974-75-3 (bevacizumab); 140608-64-6 (OKT 3); 192391-48-3
 (tositumomab i 131)

SECTION HEADINGS:

026 Immunology, Serology and Transplantation
 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index

2/9/2 (Item 2 from file: 73)

DIALOG(R)File 73:EMBASE

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13548271 EMBASE No: 2006019618

Humanized antibodies as therapeutics

ANTICORPS HUMANISES EN THERAPEUTIQUE

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 Sciences Pharmaceutiques et Biologiques de Paris, 4, avenue de
 l'Observatoire, 75006 Paris France

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Medecine/Sciences (MED. SCI.) (France) 2005, 21/12 (1054-1062)

CODEN: MSMSE ISSN: 0767-0974

DOCUMENT TYPE: Journal ; Review

LANGUAGE: FRENCH SUMMARY LANGUAGE: ENGLISH; FRENCH

NUMBER OF REFERENCES: 35

Since 1997, nine humanized antibodies received the approval of the FDA to be used as drugs for the treatment of various diseases including transplant rejections, metastatic breast and colon cancers, leukaemia, non-Hodgkin lymphomas, allergic conditions or multiple sclerosis. This review describes techniques used to engineer these antibodies and presents the recent evolutions of these techniques: SDRs grafting or << abbreviated >> CDRs grafting. Based on the illustrative examples of several antibodies, Mylotarg(R), Herceptin(R) or Xolair(R), the therapeutic effectiveness of humanized antibodies are underlined and, with the example of Tysabri(R), the sometimes dramatic adverse effects associated with their clinical use is stressed. In a second part, this review presents some future and realistic avenues to improve the effectiveness of the humanized antibodies, to decrease their immunogenicity and to reduce their cost.

BRAND NAME/MANUFACTURER NAME: mylotarg; herceptin; xolair; tysabri; reopro; rituxan; simulect; remicade; zenapax; synagis; campath; raptiva; avastin

DRUG DESCRIPTORS:

*monoclonal antibody--adverse drug reaction--ae; *monoclonal antibody--drug development--dv; *monoclonal antibody--drug therapy--dt; *monoclonal antibody--pharmacology--pd; *human monoclonal antibody--adverse drug reaction--ae; *human monoclonal antibody--drug development--dv; *human monoclonal antibody--drug therapy--dt; *human monoclonal antibody--pharmacology--pd
 gemtuzumab ozogamicin--adverse drug reaction--ae; gemtuzumab ozogamicin--drug development--dv; gemtuzumab ozogamicin--drug therapy--dt; gemtuzumab ozogamicin--pharmacology--pd; trastuzumab--adverse drug reaction--ae; trastuzumab--drug development--dv; trastuzumab--drug therapy--dt; trastuzumab--pharmacology--pd; omalizumab--adverse drug reaction--ae; omalizumab--drug development--dv; omalizumab--drug therapy--dt; omalizumab

--pharmacology--pd; natalizumab--adverse drug reaction--ae; natalizumab
 --drug development--dv; natalizumab--drug therapy--dt; natalizumab
 --pharmacology--pd; abciximab--drug development--dv; abciximab--drug
 therapy--dt; abciximab--pharmacology--pd; rituximab--drug development--dv;
 rituximab--drug therapy--dt; rituximab--pharmacology--pd; basiliximab--drug
 development--dv; basiliximab--drug therapy--dt; basiliximab--pharmacology
 --pd; infliximab--drug development--dv; infliximab--drug therapy--dt;
 infliximab--pharmacology--pd; daclizumab--drug development--dv; daclizumab
 --drug therapy--dt; daclizumab--pharmacology--pd; palivizumab--drug
 development--dv; palivizumab--drug therapy--dt; palivizumab--pharmacology
 --pd; alemtuzumab--drug development--dv; alemtuzumab--drug therapy--dt;
 alemtuzumab--pharmacology--pd; efalizumab--drug development--dv; efalizumab
 --drug therapy--dt; efalizumab--pharmacology--pd; bevacizumab--drug
 development--dv; bevacizumab--drug therapy--dt; bevacizumab--pharmacology
 --pd

MEDICAL DESCRIPTORS:

*antibody production

drug indication; food and drug administration; graft rejection--drug
 therapy--dt; breast metastasis--drug therapy--dt; colon cancer--drug
 therapy--dt; leukemia--drug therapy--dt; nonhodgkin lymphoma--drug therapy
 --dt; allergic disease--drug therapy--dt; multiple sclerosis--drug therapy
 --dt; drug efficacy; side effect--side effect--si; immunogenicity; drug
 mechanism; human; review

CAS REGISTRY NO.: 180288-69-1 (trastuzumab); 242138-07-4 (omalizumab);
 189261-10-7 (natalizumab); 143653-53-6 (abciximab); 174722-31-7 (
 rituximab); 170277-31-3 (infliximab); 188039-54-5 (palivizumab);
 216503-57-0 (alemtuzumab); 214745-43-4 (efalizumab); 216974-75-3 (
 bevacizumab)

SECTION HEADINGS:

- 016 Cancer
- 026 Immunology, Serology and Transplantation
- 030 Clinical and Experimental Pharmacology
- 037 Drug Literature Index
- 038 Adverse Reaction Titles

2/9/3 (Item 3 from file: 73)

DIALOG(R) File 73:EMBASE

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13441553 EMBASE No: 2005472129

Monoclonal antibody successes in the clinic

Reichert J.M.; Rosensweig C.J.; Faden L.B.; Dewitz M.C.

J.M. Reichert, Tufts University, Center for the Study of Drug Development
 (CSDD), 192 South Street, Boston, MA 02111 United States

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Nature Biotechnology (NAT. BIOTECHNOL.) (United States) 2005, 23/9
 (1073-1078)

CODEN: NABIF ISSN: 1087-0156

PUBLISHER ITEM IDENTIFIER: N09051073

DOCUMENT TYPE: Journal ; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 14

Most monoclonal antibodies in clinical trials are owned by small biotech
 companies. But with blockbuster-sized revenues and approval rates higher
 than those for small-molecule drugs, that all may be set to change. (c)
 2005 Nature Publishing Group.

BRAND NAME/MANUFACTURER NAME: orthoclone/Johnson and Johnson/United States;

reopro/Centocor; rituxan/Genentech/United States; herceptin/Genentech; zenapax/Hoffmann La Roche/Switzerland; simulect/Novartis/Switzerland; synagis/Medimmune/United States; mylotarg/Wyeth/United States; campath 1h/Genzyme; zevalin/Biogen Idec; tysabri/Biogen Idec/United States; humira/Abbott; bexxar/Corixa/United States; erbitux/Imclone/United States; centoxin/Centocor; bexxar/Glaxo SmithKline/United Kingdom; mississauga/ym bioscience/Canada; amg 162/Amgen/United States; HuMax CD4/Genmab/Germany; mdx 010/Medarex/United States; aurograb/neutec/United Kingdom; lucentis/Genentech; lymphocide/Immunomedics/United States; numax/Medimmune; cimzia/UCB; segard/Abbott; removab/Trion/Germany; rencarex/Wilex/Germany; remicade; raptiva; avastin; xolair; panorex; wx g250

MANUFACTURER NAMES: Johnson and Johnson/United States; Centocor; Genentech/United States; Hoffmann La Roche/Switzerland; Novartis/Switzerland; Medimmune/United States; Wyeth/United States; Genzyme; Biogen Idec/United States; Abbott; Corixa/United States; Imclone/United States; Glaxo SmithKline/United Kingdom; Medipharma/China; ym bioscience/Canada; Chugai/Japan; Abgenix/United States; Amgen/United States; Genmab/Germany; Medarex/United States; neutec/United Kingdom; Alexion/United States; Immunomedics/United States; UCB; Trion/Germany; Wilex/Germany

DRUG DESCRIPTORS:

*monoclonal antibody--clinical trial--ct; *monoclonal antibody--drug therapy--dt; *monoclonal antibody--pharmacoeconomics--pe; *monoclonal antibody--pharmacology--pd
chimeric antibody; centoxin--drug therapy--dt; human monoclonal antibody; OKT 3--drug therapy--dt; OKT 3--pharmacology--pd; adalimumab--pharmacology--pd; ibritumomab tiuxetan--drug therapy--dt; ibritumomab tiuxetan--pharmacology--pd; tositumomab i 131--drug therapy--dt; tositumomab i 131--pharmacology--pd; edrecolomab; infliximab--pharmacoeconomics--pe; infliximab--pharmacology--pd; rituximab--pharmacoeconomics--pe; rituximab--pharmacology--pd; panitumumab--clinical trial--ct; pexelizumab--clinical trial--ct; mepolizumab--clinical trial--ct; epratuzumab--clinical trial--ct; certolizumab pegol--clinical trial--ct; monoclonal antibody G250--clinical trial--ct; immunologic agent; unindexed drug; unclassified drug; abciximab; trastuzumab; daclizumab; basiliximab; palivizumab; gemtuzumab; ozogamicin; alemtuzumab; cetuximab; ranibizumab; efalizumab; bevacizumab; omalizumab

MEDICAL DESCRIPTORS:

hybridoma; drug efficacy; drug clearance; cell immortalization; septic shock--drug therapy--dt; Gram negative sepsis--drug therapy--dt; drug mechanism; drug safety; genetic engineering; biotechnology; drug approval; food and drug administration; graft rejection--drug therapy--dt; immunosuppressive treatment; nonhodgkin lymphoma--drug therapy--dt; colorectal cancer--drug therapy--dt; angiofollicular lymph node hyperplasia--drug therapy--dt; hemostasis; cancer therapy; human; nonhuman; clinical trial; review; priority journal

DRUG TERMS (UNCONTROLLED): nimotuzumab; atlizumab--drug therapy--dt; zanolimumab--clinical trial--ct; amg 162--clinical trial--ct; eculizumab--clinical trial--ct; ranibuzimab--clinical trial--ct; methicillin resistant Staphylococcus aureus monoclonal antibody--clinical trial--ct; afelimomab--clinical trial--ct; catumaxomab--clinical trial--ct; mdx 010--clinical trial--ct; respiratory syncytial pneumovirus monoclonal antibody--clinical trial--ct; orthoclone; tysabri; mississauga; HuMax CD4; aurograb; numax; cimzia; segard; removab

CAS REGISTRY NO.: 138330-99-1 (centoxin); 140608-64-6 (OKT 3); 331731-18-1 (adalimumab); 206181-63-7 (ibritumomab tiuxetan); 192391-48-3 (tositumomab i 131); 375823-41-9 (atlizumab); 170277-31-3 (infliximab); 174722-31-7 (rituximab); 339177-26-3 (panitumumab); 219685-93-5 (pexelizumab); 196078-29-2 (mepolizumab); 205923-57-5 (epratuzumab); 428863-50-7 (certolizumab pegol); 143653-53-6 (abciximab); 180288-69-1 (trastuzumab); 188039-54-5 (palivizumab); 216503-57-0 (alemtuzumab);

205923-56-4 (cetuximab); 347396-82-1 (ranibizumab); 214745-43-4 (efalizumab); 216974-75-3 (bevacizumab); 242138-07-4 (omalizumab)

SECTION HEADINGS:

016 Cancer
025 Hematology
030 Clinical and Experimental Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index

2/9/4 (Item 4 from file: 73)

DIALOG(R)File 73:EMBASE

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13310556 EMBASE No: 2005370036

Timing of the first endomyocardial biopsy in heart transplantation after induction immunosuppressive therapy - Experience from Canadian Heart Transplant Centre

Malek F.; Kaan A.; Straatman L.; Cheung A.; Ignaszewski A.; Pavel P.
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Prague 10 Czech Republic

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Casopis Lekaru Ceskych (CAS. LEK. CESK.) (Czech Republic) 2005, 144/8
(507-509)

CODEN: CLCEA ISSN: 0008-7335

DOCUMENT TYPE: Journal ; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH; SLOVAK

NUMBER OF REFERENCES: 7

Background. The exact time point at which the first endomyocardial biopsy could be safely performed after the heart transplantation has not been systematically studied. In an attempt to determine this time point in our population, the number and severity of acute rejection episodes in the first eight weeks after the heart transplantation were assessed in 91 patients who underwent the procedure at St Paul's Hospital, Vancouver between September 1996 and December 2002. Methods and Results. For the purpose of our analysis, acute rejection was defined as the grade ≥ 2 according the International Society for Heart and Lung Transplantation (ISHLT). Three hundred and sixty two endomyocardial biopsies were performed in 87 patients surviving to the first biopsy from one to eight weeks after the heart transplantation. In 85 patients who received induction immunosuppressive therapy, 13 episodes of acute rejection were identified. In two patients who did not receive the induction therapy, three episodes of acute rejection occurred. Acute rejection grade ISHLT 3 was found in 2 patients who did not receive induction therapy and in three patients who did. ISHLT grade 4 rejection occurred at weeks 5 and 7 in two patients who received induction therapy. Only one patient who received induction therapy had acute rejection within the first three weeks after the heart transplantation. Conclusions. Our analysis reveals that the frequency of acute rejection within the first eight weeks after the heart transplantation using induction therapy is low in this cohort, suggesting that the first routine endomyocardial biopsy could be delayed until the week four post-transplant.

BRAND NAME/MANUFACTURER NAME: simulect

MANUFACTURER NAMES: Sangstat; Imtix

DRUG DESCRIPTORS:

*immunosuppressive agent--drug therapy--dt

polyclonal antibody--drug therapy--dt; thymocyte antibody--drug therapy--dt

; basiliximab--drug therapy--dt; human monoclonal antibody--drug therapy
--dt

MEDICAL DESCRIPTORS:

*heart muscle biopsy; *heart transplantation; *immunosuppressive treatment
time; cardiac graft rejection--complication--co; cardiac graft rejection
--drug therapy--dt; cardiac graft rejection--prevention--pc; safety; Canada
; heart muscle injury; human; male; female; major clinical study; human
tissue; adult; article

SECTION HEADINGS:

005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery
026 Immunology, Serology and Transplantation
037 Drug Literature Index

2/9/5 (Item 5 from file: 73)

DIALOG(R)File 73:EMBASE

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12811569 EMBASE No: 2004406100

**Early experience with two-dose daclizumab in the prevention of acute
rejection in cardiac transplantation**

Joyal D.; Cantarovich M.; Cecere R.; Giannetti N.

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Clinical Transplantation (CLIN. TRANSPLANT.) (United Kingdom) 2004,
18/5 (493-496)

CODEN: CLTRE ISSN: 0902-0063

DOCUMENT TYPE: Journal ; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 15

Background: Daclizumab is a human monoclonal antibody that binds to the interleukin-2 receptor. It has been used as induction therapy in heart transplantation with repeated administrations over several weeks. At our institution, we use a two-dose regimen of daclizumab based on its extended half-life. We sought to determine the incidence of acute rejection with 2-dose daclizumab in cardiac transplantation. Methods: Eighteen consecutive heart transplants performed at a single center were analyzed retrospectively. Patients received daclizumab (2 mg/kg) within 8 h of cardiac transplantation and a second dose (1 mg/kg) 2 wk thereafter. Maintenance immunosuppression included mycophenolate mofetil, prednisone and either cyclosporine or tacrolimus, based on side-effect profile. The endpoint was the incidence of acute rejection as defined by a histologic grade > 2 according to the classification of the International Society of Heart and Lung Transplantation. Results: Four patients had acute rejections (all were 3A) during the first 3 months post-transplantation. All four patients had rejection at the first biopsy and only two had rejection thereafter. None of the rejections were hemodynamically significant and no patients were hospitalized. All except one rejection was seen in the context of low 2-h cyclosporine levels. The two-dose regimen was easier to administer on an outpatient basis and resulted in lower cost. Conclusions: This preliminary report suggests that induction therapy with a two-dose regimen of daclizumab appears to be safe and well tolerated in patients undergoing cardiac transplantation. (c) Blackwell Munksgaard, 2004.

BRAND NAME/MANUFACTURER NAME: zenapax/Hoffmann La Roche/Canada; cellcept/
Hoffmann La Roche; neoral/Novartis/Canada; simulect/Novartis/United States

MANUFACTURER NAMES: Hoffmann La Roche/Canada; Novartis/Canada; Novartis/
United States

DRUG DESCRIPTORS:

*daclizumab--drug combination--cb; *daclizumab--drug comparison--cm; *
daclizumab--drug dose--do; *daclizumab--drug therapy--dt; *daclizumab
--pharmacoeconomics--pe; *daclizumab--pharmacokinetics--pk; *daclizumab
--pharmacology--pd; *daclizumab--intravenous drug administration--iv
human monoclonal antibody--drug dose--do; human monoclonal antibody--drug
therapy--dt; interleukin 2 receptor--endogenous compound--ec; mycophenolic
acid 2 morpholinoethyl ester--adverse drug reaction--ae; mycophenolic acid
2 morpholinoethyl ester--drug combination--cb; mycophenolic acid 2
morpholinoethyl ester--drug comparison--cm; mycophenolic acid 2
morpholinoethyl ester--drug therapy--dt; mycophenolic acid 2
morpholinoethyl ester--pharmacology--pd; prednisone--drug combination--cb;
prednisone--drug therapy--dt; cyclosporin A--drug combination--cb;
cyclosporin A--drug comparison--cm; cyclosporin A--drug therapy--dt;
tsukubaenolide--drug combination--cb; tsukubaenolide--drug therapy--dt;
thymocyte antibody--drug combination--cb; thymocyte antibody--drug
comparison--cm; thymocyte antibody--drug therapy--dt; OKT 3--drug therapy
--dt; methylprednisolone--drug combination--cb; methylprednisolone--drug
therapy--dt; methylprednisolone--intravenous drug administration--iv;
basiliximab--drug dose--do; basiliximab--pharmacokinetics--pk; basiliximab
--pharmacology--pd; corticosteroid--drug combination--cb; corticosteroid
--drug comparison--cm; corticosteroid--drug therapy--dt; placebo;
everolimus--drug comparison--cm; everolimus--drug dose--do; azathioprine
--drug comparison--cm; calcineurin inhibitor

MEDICAL DESCRIPTORS:

*acute graft rejection--drug therapy--dt; *acute graft rejection
--prevention--pc; *heart transplantation
drug receptor binding; drug half life; incidence; retrospective study;
immunosuppressive treatment; disease severity; postoperative period; heart
muscle biopsy; hemodynamics; hospitalization; outpatient care; health care
cost; drug safety; drug tolerability; gastrointestinal toxicity--side
effect--si; bone marrow toxicity--side effect--si; drug cost; human;
clinical article; controlled study; article; priority journal

CAS REGISTRY NO.: 116680-01-4, 128794-94-5 (mycophenolic acid 2
morpholinoethyl ester); 53-03-2 (prednisone); 59865-13-3, 63798-73-2 (
cyclosporin A); 104987-11-3 (tsukubaenolide); 140608-64-6 (OKT 3);
6923-42-8, 83-43-2 (methylprednisolone); 159351-69-6 (everolimus);
446-86-6 (azathioprine)

SECTION HEADINGS:

- 018 Cardiovascular Diseases and Cardiovascular Surgery
- 036 Health Policy, Economics and Management
- 037 Drug Literature Index
- 038 Adverse Reaction Titles

2/9/6 (Item 6 from file: 73)

DIALOG(R)File 73:EMBASE

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12747875 EMBASE No: 2004339524

**The role of functional genomics in selecting disease targets for
antibody-based therapy**

Davis C.G.

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States

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Drug Development Research (DRUG DEV. RES.) (United States) 2004, 61/3
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Antibodies have clearly established themselves as comprising a significant segment of marketed drugs. The rapid evolution of technologies for generating antibodies and optimizing them for therapeutic applications has led to a succession of approvals over the last decade. The success of genomics in elucidating the contents of the human genome has provided a vast number of new potential targets for antibody therapy. Future development of antibody drugs will depend upon our ability to identify new targets from the tens of thousands of recently identified genes. This effort, too, will be technology-driven. This review provides a general overview of the technologies available for enabling new target selection, technologies that are collectively referred to as "functional genomics." For organizational purposes, the technologies are divided into the following broad categories: expression profiling, comparative genomics, loss of function strategies, proteomics, and computational biology. Through judicious application of combinations of these functional genomics technologies, we can anticipate a steady stream of novel well-validated targets for antibody therapy for years to come. (c) 2004 Wiley-Liss, Inc.

BRAND NAME/MANUFACTURER NAME: orthoclone okt3; reopro; rituxan; zenapax; simulect; synagis; remicade; herceptin; mylotarg; campath; zevalin; humira; xolair; bexxar; raptiva; erbitux; avastin

DRUG DESCRIPTORS:

*monoclonal antibody--drug administration--ad; *monoclonal antibody--drug development--dv; *monoclonal antibody--drug therapy--dt; *monoclonal antibody--pharmaceutics--pr; *monoclonal antibody--pharmacology--pd; *monoclonal antibody--intravenous drug administration--iv; *monoclonal antibody--subcutaneous drug administration--sc; *chimeric antibody--drug administration--ad; *chimeric antibody--drug development--dv; *chimeric antibody--drug therapy--dt; *chimeric antibody--pharmaceutics--pr; *chimeric antibody--pharmacology--pd; *chimeric antibody--intravenous drug administration--iv; *human monoclonal antibody--drug administration--ad; *human monoclonal antibody--drug development--dv; *human monoclonal antibody--drug therapy--dt; *human monoclonal antibody--pharmaceutics--pr; *human monoclonal antibody--pharmacology--pd; *human monoclonal antibody--subcutaneous drug administration--sc; *infliximab--drug administration--ad; *infliximab--drug development--dv; *infliximab--drug therapy--dt; *infliximab--pharmaceutics--pr; *infliximab--pharmacology--pd; *infliximab--intravenous drug administration--iv; *adalimumab--drug administration--ad; *adalimumab--drug development--dv; *adalimumab--drug therapy--dt; *adalimumab--pharmaceutics--pr; *adalimumab--pharmacology--pd; *adalimumab--subcutaneous drug administration--sc

DNA; complementary DNA; messenger RNA; antisense oligonucleotide; epidermal growth factor receptor 2; ribozyme; peptide library; OKT 3--drug development--dv; OKT 3--drug therapy--dt; OKT 3--pharmaceutics--pr; OKT 3--pharmacology--pd; abciximab--drug development--dv; abciximab--drug therapy--dt; abciximab--pharmaceutics--pr; abciximab--pharmacology--pd; rituximab--drug development--dv; rituximab--drug therapy--dt; rituximab--pharmaceutics--pr; rituximab--pharmacology--pd; daclizumab--drug development--dv; daclizumab--drug therapy--dt; daclizumab--pharmaceutics--pr; daclizumab--pharmacology--pd; basiliximab--drug development--dv; basiliximab--drug therapy--dt; basiliximab--pharmaceutics--pr; basiliximab--pharmacology--pd; palivizumab--drug development--dv; palivizumab--drug therapy--dt; palivizumab--pharmaceutics--pr; palivizumab--pharmacology--pd; trastuzumab--drug development--dv; trastuzumab--drug therapy--dt; trastuzumab--pharmaceutics--pr; trastuzumab--pharmacology--pd; gemtuzumab

ozogamicin--drug development--dv; gemtuzumab ozogamicin--drug therapy--dt;
 gemtuzumab ozogamicin--pharmaceutics--pr; gemtuzumab ozogamicin
 --pharmacology--pd; alemtuzumab--drug development--dv; alemtuzumab--drug
 therapy--dt; alemtuzumab--pharmaceutics--pr; alemtuzumab--pharmacology--pd;
 ibritumomab tiuxetan--drug development--dv; ibritumomab tiuxetan--drug
 therapy--dt; ibritumomab tiuxetan--pharmaceutics--pr; ibritumomab tiuxetan
 --pharmacology--pd; omalizumab--drug development--dv; omalizumab--drug
 therapy--dt; omalizumab--pharmaceutics--pr; omalizumab--pharmacology--pd;
 tositumomab i 131--drug development--dv; tositumomab i 131--drug therapy
 --dt; tositumomab i 131--pharmaceutics--pr; tositumomab i 131--pharmacology
 --pd; efalizumab--drug development--dv; efalizumab--drug therapy--dt;
 efalizumab--pharmaceutics--pr; efalizumab--pharmacology--pd; cetuximab
 --drug development--dv; cetuximab--drug therapy--dt; cetuximab
 --pharmaceutics--pr; cetuximab--pharmacology--pd; bevacizumab--drug
 development--dv; bevacizumab--drug therapy--dt; bevacizumab--pharmaceutics
 --pr; bevacizumab--pharmacology--pd

MEDICAL DESCRIPTORS:

*immunotherapy; *genomics; *proteomics
 cancer immunotherapy; immunoprophylaxis; virus infection--drug therapy--dt;
 virus infection--prevention--pc; Respiratory syncytial pneumovirus; organ
 transplantation; graft rejection--complication--co; graft rejection--drug
 therapy--dt; graft rejection--prevention--pc; nonhodgkin lymphoma--drug
 therapy--dt; rheumatoid arthritis--drug therapy--dt; Crohn disease--drug
 therapy--dt; breast cancer--drug therapy--dt; acute granulocytic leukemia
 --drug therapy--dt; chronic lymphatic leukemia--drug therapy--dt; asthma
 --drug therapy--dt; psoriasis--drug therapy--dt; colorectal cancer--drug
 therapy--dt; drug targeting; drug indication; drug approval; gene
 expression; DNA microarray; real time polymerase chain reaction; gene
 mapping; knockout mouse; RNA interference; protein DNA interaction; mass
 spectrometry; protein microarray; phage display; human genome; molecular
 biology; human; nonhuman; mouse; human cell; animal cell; embryo; review
 MEDICAL TERMS (UNCONTROLLED): functional genomics; yeast two hybrid
 analysis

CAS REGISTRY NO.: 170277-31-3 (infliximab); 331731-18-1 (adalimumab);
 9007-49-2 (DNA); 137632-09-8 (epidermal growth factor receptor 2);
 140608-64-6 (OKT 3); 143653-53-6 (abciximab); 174722-31-7 (rituximab);
 188039-54-5 (palivizumab); 180288-69-1 (trastuzumab); 216503-57-0 (
 alemtuzumab); 206181-63-7 (ibritumomab tiuxetan); 242138-07-4 (
 omalizumab); 192391-48-3 (tositumomab i 131); 214745-43-4 (efalizumab);
 205923-56-4 (cetuximab); 216974-75-3 (bevacizumab)

SECTION HEADINGS:

- 022 Human Genetics
- 026 Immunology, Serology and Transplantation
- 030 Clinical and Experimental Pharmacology
- 037 Drug Literature Index
- 039 Pharmacy

2/9/7 (Item 7 from file: 73)

DIALOG(R)File 73:EMBASE

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12747874 EMBASE No: 2004339523

**Commercial manufacturing scale formulation and analytical
 characterization of therapeutic recombinant antibodies**

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NUMBER OF REFERENCES: 98

Stable therapeutic antibody dosage forms present production technology challenges, particularly when high-concentration formulations are needed to meet the elevated dose requirements that are generally required for successful antibody therapy. Solid dosage forms, such as lyophilized powders, are generally more stable than liquid formulations. High-concentration drug products can be achieved by reconstitution of the lyophilisate in a smaller volume than its initial (pre-lyophilization) volume, but requires a significant vial overfill. High-concentration liquid formulations are becoming feasible as new techniques and technologies become available. Analytical methods to detect subtle molecular variations have been developed to demonstrate manufacturing consistency. Some molecular heterogeneity is contributed by conserved sites, such as Asn297 glycosylation and the loss of heavy chain C-terminal Lys residues. Characteristics that affect potency, stability, or immunogenicity must be elucidated for each therapeutic antibody. (c) 2004 Wiley-Liss, Inc.

BRAND NAME/MANUFACTURER NAME: orthoclone okt3; reopro; rituxan; zenapax; herceptin; remicade; simulect; synagis; mylotarg; campath; humira; zevalin
DRUG DESCRIPTORS:

*monoclonal antibody--drug administration--ad; *monoclonal antibody--drug dose--do; *monoclonal antibody--drug therapy--dt; *monoclonal antibody--pharmaceutics--pr; *monoclonal antibody--pharmacology--pd; *monoclonal antibody--intramuscular drug administration--im; *monoclonal antibody--intravenous drug administration--iv; *monoclonal antibody--subcutaneous drug administration--sc; *chimeric antibody--drug administration--ad; *chimeric antibody--drug dose--do; *chimeric antibody--drug therapy--dt; *chimeric antibody--pharmaceutics--pr; *chimeric antibody--pharmacology--pd; *chimeric antibody--intravenous drug administration--iv; *human monoclonal antibody--drug administration--ad; *human monoclonal antibody--drug dose--do; *human monoclonal antibody--drug therapy--dt; *human monoclonal antibody--pharmaceutics--pr; *human monoclonal antibody--pharmacology--pd; *human monoclonal antibody--intramuscular drug administration--im; *human monoclonal antibody--intravenous drug administration--iv; *human monoclonal antibody--subcutaneous drug administration--sc
immunoglobulin G; OKT 3--drug administration--ad; OKT 3--drug dose--do; OKT 3--drug therapy--dt; OKT 3--pharmaceutics--pr; OKT 3--pharmacology--pd; OKT 3--intravenous drug administration--iv; abciximab--drug administration--ad; abciximab--drug dose--do; abciximab--drug therapy--dt; abciximab--pharmaceutics--pr; abciximab--pharmacology--pd; abciximab--intravenous drug administration--iv; rituximab--drug administration--ad; rituximab--drug dose--do; rituximab--drug therapy--dt; rituximab--pharmaceutics--pr; rituximab--pharmacology--pd; rituximab--intravenous drug administration--iv; daclizumab--drug administration--ad; daclizumab--drug dose--do; daclizumab--drug therapy--dt; daclizumab--pharmaceutics--pr; daclizumab--pharmacology--pd; daclizumab--intravenous drug administration--iv; trastuzumab--drug administration--ad; trastuzumab--drug dose--do; trastuzumab--drug therapy--dt; trastuzumab--pharmaceutics--pr; trastuzumab--pharmacology--pd; trastuzumab--intravenous drug administration--iv; infliximab--drug administration--ad; infliximab--drug dose--do; infliximab--drug therapy--dt; infliximab--pharmaceutics--pr; infliximab--pharmacology--pd; infliximab--intravenous drug administration--iv; basiliximab--drug administration--ad; basiliximab--drug dose--do; basiliximab--drug therapy--dt; basiliximab--pharmaceutics--pr; basiliximab--pharmacology--pd; basiliximab--intravenous drug administration--iv; palivizumab--drug

administration--ad; palivizumab--drug dose--do; palivizumab--drug therapy--dt; palivizumab--pharmaceutics--pr; palivizumab--pharmacology--pd; palivizumab--intramuscular drug administration--im; gemtuzumab ozogamicin--drug administration--ad; gemtuzumab ozogamicin--drug dose--do; gemtuzumab ozogamicin--drug therapy--dt; gemtuzumab ozogamicin--pharmaceutics--pr; gemtuzumab ozogamicin--pharmacology--pd; gemtuzumab ozogamicin--intravenous drug administration--iv; alemtuzumab--drug administration--ad; alemtuzumab--drug dose--do; alemtuzumab--drug therapy--dt; alemtuzumab--pharmaceutics--pr; alemtuzumab--pharmacology--pd; alemtuzumab--intravenous drug administration--iv; adalimumab--drug administration--ad; adalimumab--drug dose--do; adalimumab--drug therapy--dt; adalimumab--pharmaceutics--pr; adalimumab--pharmacology--pd; adalimumab--subcutaneous drug administration--sc; ibritumomab tiuxetan--drug administration--ad; ibritumomab tiuxetan--drug dose--do; ibritumomab tiuxetan--drug therapy--dt; ibritumomab tiuxetan--pharmaceutics--pr; ibritumomab tiuxetan--pharmacology--pd; ibritumomab tiuxetan--intravenous drug administration--iv; insulin--drug development--dv; insulin--pharmaceutics--pr

MEDICAL DESCRIPTORS:

*immunotherapy; *drug formulation; *drug manufacture
 cancer immunotherapy; immunoprophylaxis; food and drug administration; drug approval; drug indication; organ transplantation; graft rejection
 --complication--co; graft rejection--drug therapy--dt; graft rejection--prevention--pc; percutaneous coronary intervention; coronary artery disease--drug therapy--dt; coronary artery disease--therapy--th; nonhodgkin lymphoma--drug therapy--dt; breast cancer--drug therapy--dt; rheumatoid arthritis--drug therapy--dt; Crohn disease--drug therapy--dt; virus infection--drug therapy--dt; virus infection--prevention--pc; Respiratory syncytial pneumovirus; leukemia--drug therapy--dt; chronic lymphatic leukemia--drug therapy--dt; analytic method; ultrafiltration; polyacrylamide gel electrophoresis; capillary electrophoresis; gel permeation chromatography; electrospray mass spectrometry; biotechnology; freeze drying; powder; liquid; drug efficacy; drug safety; drug storage; drug potency; drug stability; human; review

CAS REGISTRY NO.: 97794-27-9 (immunoglobulin G); 140608-64-6 (OKT 3); 143653-53-6 (abciximab); 174722-31-7 (rituximab); 180288-69-1 (trastuzumab); 170277-31-3 (infliximab); 188039-54-5 (palivizumab); 216503-57-0 (alemtuzumab); 331731-18-1 (adalimumab); 206181-63-7 (ibritumomab tiuxetan); 9004-10-8 (insulin)

SECTION HEADINGS:

- 016 Cancer
- 026 Immunology, Serology and Transplantation
- 037 Drug Literature Index
- 039 Pharmacy

2/9/8 (Item 8 from file: 73)

DIALOG(R)File 73:EMBASE

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The clinical pharmacology of therapeutic monoclonal antibodies

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NUMBER OF REFERENCES: 105

Seventeen monoclonal antibodies are currently approved in the United States for therapeutic use in organ transplantation, percutaneous coronary intervention, prophylaxis of respiratory syncytial virus disease, rheumatoid arthritis, Crohn's disease, asthma, chronic lymphocytic leukemia, acute myeloid leukemia, non-Hodgkin's lymphoma, breast cancer, and colorectal cancer. All approved antibodies are of the IgG class. Thirteen are unconjugated intact antibodies, three are intact immunoconjugates, and one is a Fab fragment. Three of the antibodies are murine, five are chimeric, eight are humanized, and one is a fully human antibody generated by phage display technology. The antigen target and the structural and binding characteristics of the antibody determine the antibody's mechanism of action, pharmacokinetics, safety, and immunogenicity. Antibodies act through multiple mechanisms that include functional modulation of the antigen, recruitment of ADCC and CDC, and delivery of radionuclide or toxin payloads to target cells. Antibody half-life is usually governed by interaction with the FcRn receptor. In some cases, the antigen may act as a sink for antibody elimination. Safety profiles are determined by the pharmacology and tissue distribution of the target antigen, antibody isotype, the antibody payload, cytokine release, hypersensitivity reactions to xenogeneic protein, and immunogenicity. Fully human antibody technology may allow development of antibodies that have reduced risks of hypersensitivity reactions and immunogenicity, thereby enhancing safety and efficacy. The exquisite target specificity of antibodies, improvements in antibody engineering technology, and the wide availability of novel and validated therapeutic targets provide many current and future opportunities for the clinical development of therapeutic antibodies. (c) 2004 Wiley-Liss, Inc.

BRAND NAME/MANUFACTURER NAME: erbitux; xolair; zevalin; campath; mylotarg; simulect; rituxan; reopro; orthoclone okt 3; avastin; bexxar; humira; synagis; zenapax; raptiva; remicade; herceptin

DRUG DESCRIPTORS:

*monoclonal antibody--adverse drug reaction--ae; *monoclonal antibody--drug administration--ad; *monoclonal antibody--drug development--dv; *monoclonal antibody--drug dose--do; *monoclonal antibody--drug therapy--dt; *monoclonal antibody--pharmacokinetics--pk; *monoclonal antibody--pharmacology--pd; *monoclonal antibody--intramuscular drug administration--im; *monoclonal antibody--intravenous drug administration--iv; *monoclonal antibody--subcutaneous drug administration--sc; *chimeric antibody--adverse drug reaction--ae; *chimeric antibody--drug administration--ad; *chimeric antibody--drug development--dv; *chimeric antibody--drug dose--do; *chimeric antibody--drug therapy--dt; *chimeric antibody--pharmacokinetics--pk; *chimeric antibody--pharmacology--pd; *chimeric antibody--intravenous drug administration--iv; *human monoclonal antibody--adverse drug reaction--ae; *human monoclonal antibody--drug administration--ad; *human monoclonal antibody--drug development--dv; *human monoclonal antibody--drug dose--do; *human monoclonal antibody--drug therapy--dt; *human monoclonal antibody--pharmacokinetics--pk; *human monoclonal antibody--pharmacology--pd; *human monoclonal antibody--intramuscular drug administration--im; *human monoclonal antibody--intravenous drug administration--iv; *human monoclonal antibody--subcutaneous drug administration--sc
immunoglobulin G; Fc receptor; cetuximab--adverse drug reaction--ae; cetuximab--drug administration--ad; cetuximab--drug development--dv; cetuximab--drug dose--do; cetuximab--drug therapy--dt; cetuximab--pharmacokinetics--pk; cetuximab--pharmacology--pd; cetuximab--intravenous drug administration--iv; omalizumab--drug administration--ad; omalizumab--drug development--dv; omalizumab--drug dose--do; omalizumab--drug therapy

--dt; omalizumab--pharmacokinetics--pk; omalizumab--pharmacology--pd;
omalizumab--subcutaneous drug administration--sc; ibritumomab tiuxetan
--adverse drug reaction--ae; ibritumomab tiuxetan--drug administration--ad;
ibritumomab tiuxetan--drug development--dv; ibritumomab tiuxetan--drug dose
--do; ibritumomab tiuxetan--drug therapy--dt; ibritumomab tiuxetan
--pharmacokinetics--pk; ibritumomab tiuxetan--pharmacology--pd; ibritumomab
tiuxetan--intravenous drug administration--iv; alemtuzumab--adverse drug
reaction--ae; alemtuzumab--drug administration--ad; alemtuzumab--drug
development--dv; alemtuzumab--drug dose--do; alemtuzumab--drug therapy--dt;
alemtuzumab--pharmacokinetics--pk; alemtuzumab--pharmacology--pd;
alemtuzumab--intravenous drug administration--iv; gemtuzumab ozogamicin
--adverse drug reaction--ae; gemtuzumab ozogamicin--drug administration--ad
; gemtuzumab ozogamicin--drug development--dv; gemtuzumab ozogamicin--drug
dose--do; gemtuzumab ozogamicin--drug therapy--dt; gemtuzumab ozogamicin
--pharmacokinetics--pk; gemtuzumab ozogamicin--pharmacology--pd; gemtuzumab
ozogamicin--intravenous drug administration--iv; basiliximab--drug
administration--ad; basiliximab--drug development--dv; basiliximab--drug
dose--do; basiliximab--drug therapy--dt; basiliximab--pharmacokinetics--pk;
basiliximab--pharmacology--pd; basiliximab--intravenous drug administration
--iv; rituximab--adverse drug reaction--ae; rituximab--drug administration
--ad; rituximab--drug development--dv; rituximab--drug dose--do; rituximab
--drug therapy--dt; rituximab--pharmacokinetics--pk; rituximab
--pharmacology--pd; rituximab--intravenous drug administration--iv;
abciximab--drug administration--ad; abciximab--drug development--dv;
abciximab--drug dose--do; abciximab--drug therapy--dt; abciximab
--pharmacokinetics--pk; abciximab--pharmacology--pd; abciximab--intravenous
drug administration--iv; OKT 3--adverse drug reaction--ae; OKT 3--drug
administration--ad; OKT 3--drug development--dv; OKT 3--drug dose--do; OKT
3--drug therapy--dt; OKT 3--pharmacokinetics--pk; OKT 3--pharmacology--pd;
OKT 3--intravenous drug administration--iv; bevacizumab--drug
administration--ad; bevacizumab--drug development--dv; bevacizumab--drug
dose--do; bevacizumab--drug therapy--dt; bevacizumab--pharmacokinetics--pk;
bevacizumab--pharmacology--pd; bevacizumab--intravenous drug administration
--iv; tositumomab i 131--adverse drug reaction--ae; tositumomab i 131--drug
administration--ad; tositumomab i 131--drug development--dv; tositumomab i
131--drug dose--do; tositumomab i 131--drug therapy--dt; tositumomab i 131
--pharmacokinetics--pk; tositumomab i 131--pharmacology--pd; tositumomab i
131--intravenous drug administration--iv; adalimumab--drug administration
--ad; adalimumab--drug development--dv; adalimumab--drug dose--do;
adalimumab--drug therapy--dt; adalimumab--pharmacokinetics--pk; adalimumab
--pharmacology--pd; adalimumab--subcutaneous drug administration--sc;
palivizumab--drug administration--ad; palivizumab--drug development--dv;
palivizumab--drug dose--do; palivizumab--drug therapy--dt; palivizumab
--pharmacokinetics--pk; palivizumab--pharmacology--pd; palivizumab
--intramuscular drug administration--im; daclizumab--drug administration
--ad; daclizumab--drug development--dv; daclizumab--drug dose--do;
daclizumab--drug therapy--dt; daclizumab--pharmacokinetics--pk; daclizumab
--pharmacology--pd; daclizumab--intravenous drug administration--iv;
efalizumab--drug administration--ad; efalizumab--drug development--dv;
efalizumab--drug dose--do; efalizumab--drug therapy--dt; efalizumab
--pharmacokinetics--pk; efalizumab--pharmacology--pd; efalizumab
--subcutaneous drug administration--sc; infliximab--drug administration--ad
; infliximab--drug development--dv; infliximab--drug dose--do; infliximab
--drug therapy--dt; infliximab--pharmacokinetics--pk; infliximab
--pharmacology--pd; infliximab--intravenous drug administration--iv;
trastuzumab--adverse drug reaction--ae; trastuzumab--drug administration
--ad; trastuzumab--drug development--dv; trastuzumab--drug dose--do;
trastuzumab--drug therapy--dt; trastuzumab--pharmacokinetics--pk;
trastuzumab--pharmacology--pd; trastuzumab--intravenous drug administration
--iv

MEDICAL DESCRIPTORS:

*immunotherapy

organ transplantation; graft rejection--complication--co; graft rejection
 --drug therapy--dt; graft rejection--prevention--pc; virus infection--drug
 therapy--dt; virus infection--prevention--pc; Respiratory syncytial
 pneumovirus; asthma--drug therapy--dt; rheumatoid arthritis--drug therapy
 --dt; psoriasis--drug therapy--dt; Crohn disease--drug therapy--dt; chronic
 lymphatic leukemia--drug therapy--dt; acute granulocytic leukemia--drug
 therapy--dt; nonhodgkin lymphoma--drug therapy--dt; breast cancer--drug
 therapy--dt; colorectal cancer--drug therapy--dt; coronary artery disease
 --drug therapy--dt; coronary artery disease--therapy--th; percutaneous
 coronary intervention; drug indication; cancer immunotherapy;
 immunoprophylaxis; phage display; transgenic mouse; chimera; immunogenicity
 ; antibody specificity; drug targeting; drug half life; drug efficacy; drug
 safety; drug hypersensitivity--side effect--si; cardiotoxicity--side effect
 --si; human; nonhuman; mouse; review

DRUG TERMS (UNCONTROLLED): orthoclone okt 3

CAS REGISTRY NO.: 97794-27-9 (immunoglobulin G); 205923-56-4 (cetuximab);
 242138-07-4 (omalizumab); 206181-63-7 (ibritumomab tiuxetan);
 216503-57-0 (alemtuzumab); 174722-31-7 (rituximab); 143653-53-6 (
 abcximab); 140608-64-6 (OKT 3); 216974-75-3 (bevacizumab); 192391-48-3
 (tositumomab i 131); 331731-18-1 (adalimumab); 188039-54-5 (palivizumab
); 214745-43-4 (efalizumab); 170277-31-3 (infliximab); 180288-69-1 (
 trastuzumab)

SECTION HEADINGS:

016 Cancer
 026 Immunology, Serology and Transplantation
 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index
 038 Adverse Reaction Titles

2/9/9 (Item 9 from file: 73)

DIALOG(R) File 73:EMBASE

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12194391 EMBASE No: 2003305675

**Treatment of graft-versus-host disease after liver transplantation with
 Basiliximab followed by bowel resection**

Sudhindran S.; Taylor A.; Delriviere L.; Collins V.P.; Liu L.; Taylor
 C.J.; Alexander G.J.; Gimson A.E.; Jamieson N.V.; Watson C.J.E.; Gibbs P.
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American Journal of Transplantation (AM. J. TRANSPLANT.) (Denmark)

2003, 3/8 (1024-1029)

CODEN: AJTMB ISSN: 1600-6135

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NUMBER OF REFERENCES: 28

Graft-versus-host disease (GVHD) after orthotopic liver transplantation
 (OLT) is a serious complication with mortality rates over 80%. Two patients
 with established GVHD after OLT were treated with Basiliximab, a chimeric
 murine human monoclonal antibody which binds to the alpha-chain of
 interleukin-2 receptor (IL-2R). Two males, aged 45 and 56 years, presented
 after OLT with a clinical picture consistent with GVHD. Quantitative
 measurements of recipient peripheral blood donor lymphocyte chimerism were
 carried out by flow cytometric analysis, and showed peak chimerism levels
 of 5% and 8%, respectively. Treatment comprised 3 doses of 1 g methyl

prednisolone followed by 2 doses of 20 mg of Basiliximab. In both, treatment resulted in complete disappearance of macro-chimerism in blood. There was resolution of skin rash by day 7; however, diarrhea persisted. White cell scan showed increased uptake in the terminal ileum and small-bowel resection was performed in both patients. One patient is alive and well 36 months after OLT. The other patient had resolution of GVHD, but died of recurrent hepatitis C 1 year after OLT. The combination of immunological and surgical treatment for GVHD following solid organ transplantation has not previously been described.

BRAND NAME/MANUFACTURER NAME: simulect/Novartis

MANUFACTURER NAMES: Novartis

DRUG DESCRIPTORS:

*basiliximab--drug combination--cb; *basiliximab--drug dose--do; *basiliximab--drug therapy--dt; *basiliximab--intravenous drug administration--iv
 immunosuppressive agent--drug combination--cb; immunosuppressive agent--drug dose--do; immunosuppressive agent--drug therapy--dt; immunosuppressive agent--intravenous drug administration--iv; steroid--drug combination--cb; steroid--drug dose--do; steroid--drug therapy--dt; steroid--intravenous drug administration--iv; prednisolone--drug combination--cb; prednisolone--drug therapy--dt; azathioprine--drug combination--cb; azathioprine--drug therapy--dt; tsukubaenolide--drug combination--cb; tsukubaenolide--drug therapy--dt; methylprednisolone--drug combination--cb; methylprednisolone--drug dose--do; methylprednisolone--drug therapy--dt; methylprednisolone--intravenous drug administration--iv; antiviral agent--drug therapy--dt; antiviral agent--oral drug administration--po; ganciclovir--drug therapy--dt; ganciclovir--oral drug administration--po; antibiotic agent--drug therapy--dt; antibiotic agent--oral drug administration--po; cotrimoxazole--drug therapy--dt; cotrimoxazole--oral drug administration--po; HLA antigen

MEDICAL DESCRIPTORS:

*liver transplantation; *intestine resection; *graft versus host reaction--complication--co; *graft versus host reaction--drug therapy--dt; *graft versus host reaction--prevention--pc
 organ transplantation; lymphocyte; chimera; flow cytometry; fluorescence in situ hybridization; liver cirrhosis--surgery--su; diarrhea--complication--co; erythema--complication--co; rash--complication--co; skin biopsy; HLA typing; X chromosome; acute graft rejection--complication--co; acute graft rejection--drug therapy--dt; acute graft rejection--prevention--pc; cytomegalovirus infection--complication--co; cytomegalovirus infection--drug therapy--dt; cytomegalovirus infection--prevention--pc; Pneumocystis carinii pneumonia--complication--co; Pneumocystis carinii pneumonia--drug therapy--dt; Pneumocystis carinii pneumonia--prevention--pc; liver function test; recurrent infection--complication--co; hepatitis C--complication--co; human; male; case report; adult; article

CAS REGISTRY NO.: 50-24-8 (prednisolone); 446-86-6 (azathioprine);

104987-11-3 (tsukubaenolide); 6923-42-8, 83-43-2 (methylprednisolone);

82410-32-0 (ganciclovir); 8064-90-2 (cotrimoxazole)

SECTION HEADINGS:

005 General Pathology and Pathological Anatomy

009 Surgery

026 Immunology, Serology and Transplantation

037 Drug Literature Index

2/9/10 (Item 10 from file: 73)

DIALOG(R)File 73:EMBASE

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11644830 EMBASE No: 2002216431

Therapeutic monoclonal antibodies: Trends in development and approval in the US

Reichert J.M.

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AUTHOR EMAIL: janice.reichert@tufts.edu

Current Opinion in Molecular Therapeutics (CURR. OPIN. MOL. THER.) (United Kingdom) 2002, 4/2 (110-118)

CODEN: CUOTF ISSN: 1464-8431

DOCUMENT TYPE: Journal ; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 39

Monoclonal antibodies have significant potential as therapeutic agents because of their ability to bind to specific antigens. To determine trends in the clinical development and approval processes for therapeutic mAbs, data on 199 mAbs that entered clinical study from 1980 to 2001 were collected and analyzed. Of the 199 mAbs, 75 are in clinical development, two are undergoing Food and Drug Administration (FDA) review, and 11 are FDA approved. Approval success rates for murine, chimeric and humanized mAbs, and clinical and approval phase lengths for mAbs, are presented. In addition, mAbs that are either in phase III, FDA-review, or are FDA approved for antineoplastic or immunological indications are described.

BRAND NAME/MANUFACTURER NAME: remicade/Centocor; xolair/Genentech; orthoclone/Johnson and Johnson; OKT 3/Johnson and Johnson; zenapax/Protein Design; simulect/Novartis; ceavac

MANUFACTURER NAMES: Ilex Oncology; Burroughs Wellcome; BTG; Leukosite; Millennium Pharmaceuticals; Centocor; Medimmune; Genentech; Johnson and Johnson; Protein Design; Novartis

DRUG DESCRIPTORS:

*monoclonal antibody--adverse drug reaction--ae; *monoclonal antibody--drug combination--cb; *monoclonal antibody--drug development--dv; *monoclonal antibody--drug therapy--dt; *monoclonal antibody--pharmacokinetics--pk; *monoclonal antibody--pharmacology--pd; *chimeric antibody--drug combination--cb; *chimeric antibody--drug development--dv; *chimeric antibody--drug therapy--dt; *chimeric antibody--pharmacology--pd; *human monoclonal antibody--adverse drug reaction--ae; *human monoclonal antibody--drug combination--cb; *human monoclonal antibody--drug development--dv; *human monoclonal antibody--drug therapy--dt; *human monoclonal antibody--pharmacology--pd

recombinant protein--adverse drug reaction--ae; recombinant protein--drug combination--cb; recombinant protein--drug development--dv; recombinant protein--drug therapy--dt; recombinant protein--pharmacology--pd; alemtuzumab--drug development--dv; alemtuzumab--drug therapy--dt; alemtuzumab--pharmacology--pd; antineoplastic agent--adverse drug reaction--ae; antineoplastic agent--drug combination--cb; antineoplastic agent--drug development--dv; antineoplastic agent--drug therapy--dt; immunologic agent--drug development--dv; immunologic agent--drug therapy--dt; abciximab--drug development--dv; abciximab--drug therapy--dt; abciximab--pharmacology--pd; palivizumab--drug development--dv; palivizumab--drug therapy--dt; palivizumab--pharmacology--pd; capecitabine--drug combination--cb; capecitabine--drug therapy--dt; cancer vaccine--drug development--dv; cancer vaccine--pharmacology--pd; cetuximab--drug development--dv; cetuximab--drug therapy--dt; cetuximab--pharmacology--pd; irinotecan--drug therapy--dt; gemtuzumab ozogamicin--drug development--dv; gemtuzumab ozogamicin--drug therapy--dt; gemtuzumab ozogamicin--pharmacology--pd; tositumomab--drug development--dv; tositumomab--drug therapy--dt; tositumomab--pharmacology--pd; epratuzumab--drug development--dv;

epratuzumab--pharmacology--pd; rituximab--drug combination--cb; rituximab
 --drug development--dv; rituximab--drug therapy--dt; rituximab
 --pharmacology--pd; ibritumomab tiuxetan--drug development--dv; ibritumomab
 tiuxetan--drug therapy--dt; ibritumomab tiuxetan--pharmacology--pd;
 cyclophosphamide--drug combination--cb; cyclophosphamide--drug therapy--dt;
 doxorubicin--drug combination--cb; doxorubicin--drug therapy--dt;
 vincristine--drug combination--cb; vincristine--drug therapy--dt;
 prednisone--drug combination--cb; prednisone--drug therapy--dt; trastuzumab
 --adverse drug reaction--ae; trastuzumab--drug combination--cb; trastuzumab
 --drug development--dv; trastuzumab--drug therapy--dt; trastuzumab
 --pharmacology--pd; omalizumab--drug development--dv; omalizumab--drug
 therapy--dt; omalizumab--pharmacology--pd; interleukin 2 receptor antibody
 --drug combination--cb; interleukin 2 receptor antibody--drug development
 --dv; interleukin 2 receptor antibody--drug therapy--dt; interleukin 2
 receptor antibody--pharmacology--pd; infliximab--drug development--dv;
 infliximab--drug therapy--dt; infliximab--pharmacology--pd; OKT 3--drug
 development--dv; OKT 3--drug therapy--dt; OKT 3--pharmacology--pd;
 fludarabine--drug therapy--dt; alkylating agent--drug therapy--dt;
 unindexed drug

MEDICAL DESCRIPTORS:

drug approval; antigen antibody complex; food and drug administration;
 cancer--drug therapy--dt; immunotherapy; drug indication; graft rejection
 --complication--co; graft rejection--drug therapy--dt; graft rejection
 --prevention--pc; drug half life; drug efficacy; sepsis--drug therapy--dt;
 heart muscle ischemia--drug therapy--dt; lower respiratory tract infection
 --drug therapy--dt; cardiotoxicity--side effect--si; allergic rhinitis
 --drug therapy--dt; autoimmune disease--drug therapy--dt; human; controlled
 study; adult; article

DRUG TERMS (UNCONTROLLED): orthoclone; ceavac

CAS REGISTRY NO.: 216503-57-0 (alemtuzumab); 143653-53-6 (abciximab);
 188039-54-5 (palivizumab); 154361-50-9 (capecitabine); 205923-56-4 (
 cetuximab); 100286-90-6 (irinotecan); 208921-02-2 (tositumomab);
 205923-57-5 (epratuzumab); 174722-31-7 (rituximab); 206181-63-7 (
 ibritumomab tiuxetan); 50-18-0 (cyclophosphamide); 23214-92-8,
 25316-40-9 (doxorubicin); 57-22-7 (vincristine); 53-03-2 (prednisone);
 180288-69-1 (trastuzumab); 242138-07-4 (omalizumab); 179045-86-4 (
 interleukin 2 receptor antibody); 170277-31-3 (infliximab); 140608-64-6
 (OKT 3); 21679-14-1 (fludarabine)

SECTION HEADINGS:

026 Immunology, Serology and Transplantation
 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index
 038 Adverse Reaction Titles

2/9/11 (Item 11 from file: 73)

DIALOG(R)File 73:EMBASE

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11297016 EMBASE No: 2001311277

Monoclonal antibodies in the clinic

Reichert J.M.

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Nature Biotechnology (NAT. BIOTECHNOL.) (United States) 2001, 19/9
 (819-822)

CODEN: NABIF ISSN: 1087-0156

DOCUMENT TYPE: Journal ; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 8

Despite initial teething problems, the number of clinically effective monoclonal antibodies is growing.

BRAND NAME/MANUFACTURER NAME: orthoclone/Ortho; reopro/Centocor; rituxan/Genentech; zenapax/Hoffmann La Roche; simulect/Novartis; synagis/Medimmune; remicade/Centocor; herceptin/Genentech; mylotarg/Wyeth Ayerst; campath/Millennium

MANUFACTURER NAMES: Ortho; Centocor; Genentech; Hoffmann La Roche; Novartis; Medimmune; Wyeth Ayerst; Millennium

DRUG DESCRIPTORS:

*monoclonal antibody--clinical trial--ct; *monoclonal antibody--drug development--dv

OKT 3; chimeric antibody; human monoclonal antibody--drug development--dv; abciximab; rituximab; interleukin 2 receptor antibody; palivizumab; infliximab; trastuzumab; gemtuzumab ozogamicin; unclassified drug

MEDICAL DESCRIPTORS:

hybridoma; B lymphocyte; immunogenicity; hybrid cell; immunosurveillance; antigenicity; phage display; drug approval; clinical research; drug research; human; nonhuman; clinical trial; review; priority journal

DRUG TERMS (UNCONTROLLED): alemtuzumab; orthoclone; campath

CAS REGISTRY NO.: 140608-64-6 (OKT 3); 143653-53-6 (abciximab); 174722-31-7 (rituximab); 179045-86-4 (interleukin 2 receptor antibody); 188039-54-5 (palivizumab); 170277-31-3 (infliximab); 180288-69-1 (trastuzumab)

SECTION HEADINGS:

026 Immunology, Serology and Transplantation

037 Drug Literature Index

2/9/12 (Item 12 from file: 73)

DIALOG(R)File 73:EMBASE

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10900692 EMBASE No: 2000381566

Immunogenicity: The last hurdle for clinically successful therapeutic antibodies

Adair F.

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BioPharm (BIOPHARM) (United States) 2000, 13/10 (42-44+46)

CODEN: BPRME ISSN: 1040-8304

DOCUMENT TYPE: Journal; Review

LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 12

BRAND NAME/MANUFACTURER NAME: rituxan; simulect; remicade

DRUG DESCRIPTORS:

*antibody--drug analysis--an; *antibody--pharmaceutics--pr; *antibody--pharmacology--pd

human monoclonal antibody--drug analysis--an; human monoclonal antibody--pharmaceutics--pr; human monoclonal antibody--pharmacology--pd; rituximab--drug analysis--an; rituximab--pharmaceutics--pr; rituximab--pharmacology--pd; infliximab--drug analysis--an; infliximab--pharmaceutics--pr; infliximab--pharmacology--pd; interleukin 2 receptor antibody--drug analysis--an; interleukin 2 receptor antibody--pharmaceutics--pr; interleukin 2 receptor antibody--pharmacology--pd; monoclonal antibody B.72.3--drug analysis--an; monoclonal antibody B.72.3--pharmaceutics--pr; monoclonal antibody B.72.3--pharmacology--pd; chimeric antibody--drug analysis--an; chimeric antibody--pharmaceutics--pr; chimeric antibody

--pharmacology--pd; CD52 antigen--endogenous compound--ec; interleukin 2
receptor--endogenous compound--ec; major histocompatibility antigen class 2
--endogenous compound--ec; Fc receptor--endogenous compound--ec; T
lymphocyte receptor--endogenous compound--ec; unclassified drug

MEDICAL DESCRIPTORS:

*drug antigenicity; *antibody production
immunotherapy; drug purification; drug manufacture; immunomodulation;
computer simulation; immunological tolerance; peptide analysis; artificial
neural network; human; nonhuman; review

DRUG TERMS (UNCONTROLLED): monoclonal antibody campath 1h--drug analysis
--an; monoclonal antibody campath 1h--pharmaceutics--pr; monoclonal
antibody campath 1h--pharmacology--pd; monoclonal antibody nr lu 13--drug
analysis--an; monoclonal antibody nr lu 13--pharmaceutics--pr; monoclonal
antibody nr lu 13--pharmacology--pd

CAS REGISTRY NO.: 174722-31-7 (rituximab); 170277-31-3 (infliximab);
179045-86-4 (interleukin 2 receptor antibody)

SECTION HEADINGS:

036 Health Policy, Economics and Management
037 Drug Literature Index
039 Pharmacy

?

S DACLIZUMAB AND (TAC OR (IL (W) 2) AND ANTIBODY

>>>Unmatched parentheses

?

S DACLIZUMAB AND (TAC OR (IL (W) 2)) AND ANTIBODY

Processing

Processing

Processing

Processed 10 of 10 files ...

Completed processing all files

2815 DACLIZUMAB

18187 TAC

695923 IL

15349961 2

159581 IL(W)2

1769948 ANTIBODY

S3 305 DACLIZUMAB AND (TAC OR (IL (W) 2)) AND ANTIBODY

?

S S3 AND (HUMAN (W) MONOCLONAL)

Processing

Processing

Processing

Processed 10 of 10 files ...

Completed processing all files

305 S3

17510383 HUMAN

850917 MONOCLONAL

15734 HUMAN(W) MONOCLONAL

S4 0 S3 AND (HUMAN (W) MONOCLONAL)

?

?

Set	Items	Description
S1	12	SIMULECT AND (HUMAN (W) MONOCLONAL (W) ANTIBODY)
S2	12	RD S1 (unique items)
S3	305	DACLIZUMAB AND (TAC OR (IL (W) 2)) AND ANTIBODY
S4	0	S3 AND (HUMAN (W) MONOCLONAL)

?

S S3 AND (HUMAN (1W) ANTIBODY)

Processing

Processing

Processed 10 of 10 files ...

Completed processing all files

	305	S3
	17510383	HUMAN
	1769948	ANTIBODY
	21334	HUMAN(1W)ANTIBODY
S5	0	S3 AND (HUMAN (1W) ANTIBODY)

?

?

Set	Items	Description
S1	12	SIMULECT AND (HUMAN (W) MONOCLONAL (W) ANTIBODY)
S2	12	RD S1 (unique items)
S3	305	DACLIZUMAB AND (TAC OR (IL (W) 2)) AND ANTIBODY
S4	0	S3 AND (HUMAN (W) MONOCLONAL)
S5	0	S3 AND (HUMAN (1W) ANTIBODY)

?

S S3 AND HUMAN

Processing

Processed 10 of 10 files ...

Completed processing all files

	305	S3
	17510383	HUMAN
S6	210	S3 AND HUMAN

?

DS

Set	Items	Description
S1	12	SIMULECT AND (HUMAN (W) MONOCLONAL (W) ANTIBODY)
S2	12	RD S1 (unique items)
S3	305	DACLIZUMAB AND (TAC OR (IL (W) 2)) AND ANTIBODY
S4	0	S3 AND (HUMAN (W) MONOCLONAL)
S5	0	S3 AND (HUMAN (1W) ANTIBODY)
S6	210	S3 AND HUMAN
?		

S S6 AND (IL (W) 2 (W) BINDING)

Processing

Processing

Processing

Processed 10 of 10 files ...

Completed processing all files

210	S6
695923	IL
15349961	2
3205298	BINDING
1598	IL(W)2(W)BINDING
S7	3 S6 AND (IL (W) 2 (W) BINDING)

?

?

RD S7

S8 3 RD S7 (unique items)

?

TYPE S8/FULL/1-3

8/9/1 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0015573239 BIOSIS NO.: 200510267739

Daclizumab therapy improves outcome in steroid refractory acute graft versus host disease (aGVHD).

AUTHOR: Doocey Richard T (Reprint); Greenwood Matthew J; Warkentin Dawn; Song Kevin W; Le Alan; Nitta Janet; Nevill Thomas J; Barnett Michael J; Forrest Donna L; Hogge Donna E; Lavoie Julye C; Nantel Stephen H; Shepherd John D; Sutherland Heather J; Toze Cynthia L; Smith Clayton A

AUTHOR ADDRESS: Vancouver Gen Hosp, Leukemia Bone Marrow Transplant Program
British C, Vancouver, BC, Canada**Canada

JOURNAL: Blood 104 (11, Part 2): p356B NOV 16 2004 2004

CONFERENCE/MEETING: 46th Annual Meeting of the
American-Society-of-Hematology San Diego, CA, USA December 04 -07, 2004;

20041204

SPONSOR: Amer Soc Hematol

ISSN: 0006-4971

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Steroid refractory aGVHD following allogeneic stem cell transplant (SCT) is associated with a long-term event-free survival (EFS) of less than 20%. Daclizumab is a humanised monoclonal antibody specific for the Tac subunit of the Interleukin-2 (IL-2) receptor. It inhibits IL-2 binding and is thought to be more specific for alloreactive lymphocytes than pan-T cell antibodies. Limited phase I trials using daclizumab for steroid refractory aGVHD have demonstrated 50-60% complete response (CR) rates, though its safety and efficacy as primary aGVHD treatment has recently been questioned. We examined the Vancouver experience with daclizumab in the management of steroid refractory aGVHD. Between 8/00 and 2/04, 35 patients with steroid refractory aGVHD were treated with daclizumab. Male:female ratio was 1.7:1. Median age was 42 years (17-53). Pretransplant diagnoses were AML (n=7), ALL (n=6), CML (n=6), MDS (n=5), NHL (n=6), MM (n=4) and Myelofibrosis (n=1). One patient with relapsed AML post-SCT developed aGVHD following DLI. Stem cell source was matched unrelated bone marrow (BM) (n=11) or peripheral blood (PB) (n=8), mismatched unrelated BM (n=6) or PB (n=3), matched related BM (n=2) or PB (n=4), and mismatched related BM (n=1). Twenty eight pts were conditioned with Cyclophosphamide/TBI. CSP/MTX aGVHD prophylaxis was used in all pts and initial aGVHD therapy consisted of Methylprednisolone 2 mg/kg IV. Grade I-II aGVHD developed in 18/35 (51%) pts and grade III-IV in 17/35 (49%) pts. Median onset of aGVHD was 18 (6-49) days post transplant. Steroid refractory pts received daclizumab 1 mg/kg IV (maximum dose 100mg) on days 1, 4, 8, 15 and 22 at a median of 40 (18-94) days post transplant. Daclizumab response was assessed at day 42 following its initiation. A CR was defined as a return to stage/grade 0 aGVHD and a PR as a reduction of ≥ 1 aGVHD stage/grade without need for additional therapy. There were no significant infusional complications. One patient died during the response assessment period (regimen related pulmonary toxicity). Overall response rate (ORR) was 25/35 (73%), with 15/25 (44%) achieving a CR and 10/25 (29%) a PR. Response was most likely in pts with skin involvement. [GRAPHICS] Twenty four (68%) pts developed limited (n=8) or extensive (n=15) chronic GVHD. The 3-year OS and EFS rates were 35% (95% CI 17-53%) and 28% (95% CI 12-47%), respectively. Female patients had a significantly poorer OS ($p=0.0064$) and EFS ($p=0.0112$) as did those pts receiving SCT from female donors ($p=0.0333/0.0456$). Eleven patients (31%) received antithymocyte globulin (ATG) in addition to daclizumab. In this subgroup, aGVHD response was more likely but ATG treated patients had increased CMV antigenemia rates during the treatment response period ($p=0.01$), and a significantly lower EFS ($p=0.0064$) and OS ($p=0.0123$). Daclizumab is an effective agent for steroid refractory aGVHD especially if limited to the skin. Long-term survival appears to be superior in pts treated with this agent although its use along with ATG may compromise pt outcome.

REGISTRY NUMBERS: 50-18-0: cyclophosphamide; 152923-56-3: daclizumab;
83-43-2: methylprednisolone

DESCRIPTORS:

MAJOR CONCEPTS: Pharmacology; Clinical Immunology--Human Medicine,
Medical Sciences; Hematology--Human Medicine, Medical Sciences

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata,
Animalia

ORGANISMS: human (Hominidae)--adolescent, middle age, adult, female,

male

ORGANISMS: PARTS ETC: peripheral blood--blood and lymphatics

COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

DISEASES: non-Hodgkin's lymphoma--neoplastic disease, immune system disease, blood and lymphatic disease; chronic myeloid leukemia--neoplastic disease, blood and lymphatic disease; acute myeloid leukemia--neoplastic disease, blood and lymphatic disease; myelofibrosis--blood and lymphatic disease; myelodysplastic syndrome--neoplastic disease, blood and lymphatic disease; acute graft-vs-host disease--immune system disease

MESH TERMS: Leukemia, Myeloid, Chronic (MeSH); Leukemia, Myeloid (MeSH); Myelofibrosis (MeSH); Myelodysplastic Syndromes (MeSH); Graft vs Host Disease (MeSH)

CHEMICALS & BIOCHEMICALS: cyclophosphamide--antineoplastic-drug, hematologic-drug, immunologic-drug; daclizumab--immunologic-drug, immunosuppressant-drug; methylprednisolone--antineoplastic-drug, autonomic-drug; multiple myeloma

CONCEPT CODES:

00520 General biology - Symposia, transactions and proceedings
 10060 Biochemistry studies - General
 10067 Biochemistry studies - Sterols and steroids
 12512 Pathology - Therapy
 15002 Blood - Blood and lymph studies
 15004 Blood - Blood cell studies
 15006 Blood - Blood, lymphatic and reticuloendothelial pathologies
 22002 Pharmacology - General
 22005 Pharmacology - Clinical pharmacology
 22008 Pharmacology - Blood and hematopoietic agents
 22018 Pharmacology - Immunological processes and allergy
 22024 Pharmacology - Neuropharmacology
 24004 Neoplasms - Pathology, clinical aspects and systemic effects
 24008 Neoplasms - Therapeutic agents and therapy
 24010 Neoplasms - Blood and reticuloendothelial neoplasms
 25000 Pediatrics
 34508 Immunology - Immunopathology, tissue immunology

BIOSYSTEMATIC CODES:

86215 Hominidae

8/9/2 (Item 1 from file: 73)

DIALOG(R)File 73:EMBASE

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11849195 EMBASE No: 2002422735

The use of basiliximab in solid organ transplantation

Henry M.L.; Rajab A.

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Expert Opinion on Pharmacotherapy (EXPERT OPIN. PHARMACOTHER.) (United Kingdom) 01 NOV 2002, 3/11 (1657-1663)

CODEN: EOPHF ISSN: 1465-6566

DOCUMENT TYPE: Journal ; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 38

The risk of acute rejection is at its highest early post-transplant. The use of various antibodies early after transplant achieves potent

immunosuppression to prevent acute rejection, allowing the clinician the opportunity to optimise baseline immunosuppressive management and to delay the use of nephrotoxic agents (calcineurin inhibitors), while the graft reaches a baseline function. Basiliximab (Simulect(TM), Novartis) is a monoclonal antibody that binds specifically to the alpha-subunit of the human high-affinity interleukin-2 receptor (IL-2r) complex, consequently inhibiting interleukin-2 (IL-2) binding. IL-2 receptors are selectively expressed on the surface of the activated lymphocytes. Administration of basiliximab inhibits IL-2 mediated activation of lymphocytes, a critical pathway involved in allograft rejection. Several clinical studies have shown that basiliximab administration as an induction agent significantly reduces the incidence of acute rejection, even in high risk patients. In addition, basiliximab is well-tolerated with minimal side effects.

BRAND NAME/MANUFACTURER NAME: neoral/Novartis; simulect/Novartis; atgam/Upjohn; orthoclone/Ortho; zenapax/Hoffmann La Roche

MANUFACTURER NAMES: Novartis; Upjohn; Ortho; Hoffmann La Roche

DRUG DESCRIPTORS:

*basiliximab--adverse drug reaction--ae; *basiliximab--clinical trial--ct; *basiliximab--drug combination--cb; *basiliximab--drug comparison--cm; *basiliximab--drug concentration--cr; *basiliximab--drug development--dv; *basiliximab--drug dose--do; *basiliximab--drug therapy--dt; *basiliximab--pharmacoeconomics--pe; *basiliximab--pharmacokinetics--pk; *basiliximab--pharmacology--pd; *basiliximab--intravenous drug administration--iv; *basiliximab--subconjunctival drug administration--cj
antibody; calcineurin inhibitor--adverse drug reaction--ae; monoclonal antibody--drug therapy--dt; monoclonal antibody--pharmacology--pd; interleukin 2 receptor--endogenous compound--ec; interleukin 2--endogenous compound--ec; chimeric antibody--adverse drug reaction--ae; chimeric antibody--clinical trial--ct; chimeric antibody--drug combination--cb; chimeric antibody--drug comparison--cm; chimeric antibody--drug concentration--cr; chimeric antibody--drug development--dv; chimeric antibody--drug dose--do; chimeric antibody--drug therapy--dt; chimeric antibody--pharmacoeconomics--pe; chimeric antibody--pharmacokinetics--pk; chimeric antibody--pharmacology--pd; daclizumab--drug combination--cb; daclizumab--drug development--dv; daclizumab--drug dose--do; daclizumab--drug therapy--dt; daclizumab--pharmacology--pd; immunoglobulin G--endogenous compound--ec; immunoglobulin F(ab) fragment--endogenous compound--ec; placebo; cyclosporin--drug combination--cb; cyclosporin--drug therapy--dt; corticosteroid--drug combination--cb; corticosteroid--drug therapy--dt; steroid--drug combination--cb; steroid--drug therapy--dt; azathioprine--drug combination--cb; azathioprine--drug therapy--dt; thymocyte antibody--drug comparison--cm; thymocyte antibody--drug therapy--dt; thymocyte antibody--pharmacoeconomics--pe; thymocyte antibody--pharmacology--pd; OKT 3--adverse drug reaction--ae; OKT 3--clinical trial--ct; OKT 3--drug comparison--cm; OKT 3--drug therapy--dt; cytokine--endogenous compound--ec; tsukubaenolide--drug comparison--cm; tsukubaenolide--drug therapy--dt; mycophenolic acid 2 morpholinoethyl ester--drug combination--cb; mycophenolic acid 2 morpholinoethyl ester--drug comparison--cm; mycophenolic acid 2 morpholinoethyl ester--drug therapy--dt; polyclonal antibody--adverse drug reaction--ae; polyclonal antibody--drug comparison--cm; polyclonal antibody--drug therapy--dt; creatinine--endogenous compound--ec; immunosuppressive agent--adverse drug reaction--ae; immunosuppressive agent--clinical trial--ct; immunosuppressive agent--drug combination--cb; immunosuppressive agent--drug comparison--cm; immunosuppressive agent--drug concentration--cr; immunosuppressive agent--drug development--dv; immunosuppressive agent--drug dose--do; immunosuppressive agent--drug therapy--dt; immunosuppressive agent--pharmacoeconomics--pe; immunosuppressive agent--pharmacology--pd; immunosuppressive agent--intravenous drug administration--iv; cyclosporin A

MEDICAL DESCRIPTORS:

*acute graft rejection--diagnosis--di; *acute graft rejection--disease management--dm; *acute graft rejection--drug resistance--dr; *acute graft rejection--drug therapy--dt; *acute graft rejection--prevention--pc kidney transplantation; risk assessment; immunosuppressive treatment; graft patency; drug specificity; alpha chain; drug protein binding; protein expression; surface property; lymphocyte activation; high risk patient; drug tolerability; cytomegalovirus infection--side effect--si; drug half life; drug blood level; drug efficacy; cost effectiveness analysis; herpes simplex--side effect--si; pancreas transplantation; liver transplantation; lung edema--side effect--si; human; male; female; major clinical study; clinical trial; controlled study; aged; child; adult; review

DRUG TERMS (UNCONTROLLED): orthoclone

CAS REGISTRY NO.: 85898-30-2 (interleukin 2); 97794-27-9 (immunoglobulin G); 79217-60-0 (cyclosporin); 446-86-6 (azathioprine); 140608-64-6 (OKT 3); 104987-11-3 (tsukubaenolide); 116680-01-4, 128794-94-5 (mycophenolic acid 2 morpholinoethyl ester); 19230-81-0, 60-27-5 (creatinine); 59865-13-3, 63798-73-2 (cyclosporin A)

SECTION HEADINGS:

- 009 Surgery
- 026 Immunology, Serology and Transplantation
- 030 Clinical and Experimental Pharmacology
- 036 Health Policy, Economics and Management
- 037 Drug Literature Index
- 038 Adverse Reaction Titles

8/9/3 (Item 2 from file: 73)

DIALOG(R)File 73:EMBASE

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10828958 EMBASE No: 2000309668

Successful in vivo blockade of CD25 (high-affinity interleukin 2 receptor) on T cells by administration of humanized anti-Tac antibody to patients with psoriasis

Krueger J.G.; Walters I.B.; Miyazawa M.; Gilleaudeau P.; Hakimi J.; Light S.; Sherr A.; Gottlieb A.B.

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Journal of the American Academy of Dermatology (J. AM. ACAD. DERMATOL.) (United States) 2000, 43/3 (448-458)

CODEN: JAADD ISSN: 0190-9622

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 34

Background: Daclizumab is a humanized antibody to the alpha-subunit (CD25) of the interleukin 2 (IL-2) receptor that blocks normal IL-2 binding to this receptor. Because IL-2 is a major stimulus for T-cell growth, blockade of the IL-2 receptor could be useful in treating T-cell-mediated (autoimmune) diseases. Objective: Our purpose was to determine whether adequate concentrations of antibody were achieved in circulating blood and in psoriatic skin lesions to saturate CD25 receptors. We also intended to measure clinical effect and safety of this agent when used alone (without other immunosuppressive drugs) in psoriasis. Methods: Nineteen patients with psoriasis in two centers received daclizumab at an initial dose of 2 mg/kg, then 1 mg/kg at weeks 2, 4, 8, and 12. To determine whether CD25 was blocked in vivo, flow cytometric studies measured (1) expression of CD25 on

CD3sup + T cells derived from blood and (2) immunohistochemistry measures of CD25sup + cells done on pretreatment and posttreatment biopsy specimens. Patients were followed up clinically with photographs and Psoriasis Area and Severity Index scores. Results: This study showed a consistent blockade of CD25 in peripheral blood and tissue during the first 4 weeks of therapy while the dosing was every 2 weeks. Variable desaturation of receptors began after 4 weeks, which correlated with a reversal in disease improvement. Patients with a pretreatment Psoriasis Area and Severity Index score of less than 36 showed a mean reduction in severity by 30% at 8 weeks (P = .02). During the 16 weeks of treatment, a 44.8% decrease in expression of the IL-2 receptor alpha-subunit was found. The absolute T-cell counts were calculated and showed no significant changes during the course of the study. No significant adverse events were produced by daclizumab during this study. Conclusion: We therefore conclude that daclizumab is a well-tolerated agent that blocks CD25 expression in peripheral blood and skin. Furthermore, it may be useful in treating psoriasis in some patients.

DRUG DESCRIPTORS:

*interleukin 2 receptor--endogenous compound--ec; *interleukin 2 receptor antibody--clinical trial--ct; *interleukin 2 receptor antibody--drug therapy--dt

CD3 antigen--endogenous compound--ec

MEDICAL DESCRIPTORS:

*psoriasis--drug therapy--dt

drug efficacy; immunomodulation; receptor blocking; T lymphocyte; lymphocyte count; human; male; female; clinical article; clinical trial; multicenter study; controlled study; adult; article; priority journal

CAS REGISTRY NO.: 179045-86-4 (interleukin 2 receptor antibody)

SECTION HEADINGS:

013 Dermatology and Venereology

026 Immunology, Serology and Transplantation

037 Drug Literature Index

?

Set	Items	Description
S1	12	SIMULECT AND (HUMAN (W) MONOCLONAL (W) ANTIBODY)
S2	12	RD S1 (unique items)
S3	305	DACLIZUMAB AND (TAC OR (IL (W) 2)) AND ANTIBODY
S4	0	S3 AND (HUMAN (W) MONOCLONAL)
S5	0	S3 AND (HUMAN (1W) ANTIBODY)
S6	210	S3 AND HUMAN
S7	3	S6 AND (IL (W) 2 (W) BINDING)
S8	3	RD S7 (unique items)

?

S (HUMAN (W) MONOCLONAL (W) ANTIBODY)

Processing

Processed 10 of 10 files ...

Completed processing all files

17510383 HUMAN

850917 MONOCLONAL

1769948 ANTIBODY

S9 6876 (HUMAN (W) MONOCLONAL (W) ANTIBODY)

?

Set	Items	Description
S1	12	SIMULECT AND (HUMAN (W) MONOCLONAL (W) ANTIBODY)
S2	12	RD S1 (unique items)

S3 305 DACLIZUMAB AND (TAC OR (IL (W) 2)) AND ANTIBODY
 S4 0 S3 AND (HUMAN (W) MONOCLONAL)
 S5 0 S3 AND (HUMAN (1W) ANTIBODY)
 S6 210 S3 AND HUMAN
 S7 3 S6 AND (IL (W) 2 (W) BINDING)
 S8 3 RD S7 (unique items)
 S9 6876 (HUMAN (W) MONOCLONAL (W) ANTIBODY)
 ?

S (CD25 OR TAC OR (IL (W) 2 (W) RECEPTOR))

Processing

Processing

Processed 10 of 10 files ...

Completed processing all files

26193 CD25
 18187 TAC
 695923 IL
 15349961 2
 3130415 RECEPTOR
 22400 IL(W)2(W)RECEPTOR
 S10 61840 (CD25 OR TAC OR (IL (W) 2 (W) RECEPTOR))

?

Set	Items	Description
S1	12	SIMULECT AND (HUMAN (W) MONOCLONAL (W) ANTIBODY)
S2	12	RD S1 (unique items)
S3	305	DACLIZUMAB AND (TAC OR (IL (W) 2)) AND ANTIBODY
S4	0	S3 AND (HUMAN (W) MONOCLONAL)
S5	0	S3 AND (HUMAN (1W) ANTIBODY)
S6	210	S3 AND HUMAN
S7	3	S6 AND (IL (W) 2 (W) BINDING)
S8	3	RD S7 (unique items)
S9	6876	(HUMAN (W) MONOCLONAL (W) ANTIBODY)
S10	61840	(CD25 OR TAC OR (IL (W) 2 (W) RECEPTOR))

?

S S9 AND S10

6876 S9
 61840 S10
 S11 27 S9 AND S10

?

RD S11

S12 25 RD S11 (unique items)

?

TYPE S12/FULL/1-25

12/9/1 (Item 1 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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12957605 PMID: 11105946

Morphologic and immunohistochemical features of experimentally induced allergic contact dermatitis in Gottingen minipigs.

Vana G; Meingassner J G

Novartis Forschungsinstitut, Vienna, Austria.

Veterinary pathology (UNITED STATES) Nov 2000, 37 (6) p565-80,

ISSN 0300-9858--Print Journal Code: 0312020

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Many preclinical studies in investigative dermatology are performed preferably in pigs because pig skin is more similar to human skin than is rodent skin. A frequently used model is allergic contact dermatitis (ACD); however, this T-cell-mediated skin condition so far is not well characterized in pigs. The present study is aimed at the evaluation of morphologic and immunohistochemical features of experimentally induced acute ACD in Gottingen minipigs using 2,4-dinitrofluorobenzene (DNFB) as a hapten. Eight minipigs were sensitized with 10% DNFB and challenged 2 weeks later at different sites with 1% DNFB. In addition to clinical examinations, cutaneous blood flow was quantified by laser Doppler velocimetry (Periflux PF3). These examinations were performed before challenge and 8, 24, 48, and 72 hours after challenge. Skin biopsies were taken at the same time points, fixed, sectioned, and stained with Giemsa for histologic evaluation, or with mouse anti-swine monoclonal antibodies (CD1, CD2, CD4, CD5, CD8, CD25, CD45, MHCII) and with one mouse anti-human monoclonal antibody (CD62E) cross-reacting with swine for immunohistochemical evaluation. Positively stained cells were counted per square millimeter of epidermis and dermis by using a video image analyzing system (Videoplan Kontron). Erythema and cutaneous blood flow peaked at 24 hours. The major epidermal changes most pronounced at 48 hours were acanthosis, spongiosis, intracellular edema, exocytosis, and abscesses mainly containing neutrophils and mononuclear cells (MNC). Perivascular infiltrates of MNC as well as neutrophils and eosinophils were the most significant dermal changes, with peak levels at 24-48 hours. In biopsies taken before challenge, CD1+ dendritic cells were found in similar numbers and locations as MHCII+ cells in the epidermis. In the epidermis the maximum CD1+ cell decrease occurred at 24 hours whereas in the dermis the maximum increase in CD1+ stained cells was seen at 72 hours. The dermal infiltrate (CD2+, CD5+, CD25+, and CD45+) was most dense at 48 hours. Between 8 and 48 hours more CD4+ were present than CD8+ cells, whereas at 72 hours CD4+ and CD8+ cells were similar in numbers. These findings closely resemble changes in human ACD. Therefore, DNFB-induced ACD in Gottingen minipigs is considered to be an appropriate animal model to study immunopathologic mechanisms and pharmacologic intervention.

Tags: Female

Descriptors: *Dermatitis, Allergic Contact--immunology--IM; *Dermatitis, Allergic Contact--pathology--PA; *Disease Models, Animal; *Swine, Miniature ; Animals; Antigens, CD--analysis--AN; Dinitrofluorobenzene; Immunohistochemistry; Microcirculation--drug effects--DE; Regional Blood Flow--drug effects--DE; Skin--pathology--PA; Swine; Time Factors

CAS Registry No.: 0 (Antigens, CD); 70-34-8 (Dinitrofluorobenzene)

Record Date Created: 20010228

Record Date Completed: 20010329

12/9/2 (Item 2 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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09133642 PMID: 14621841

Prophylactic use of the IL-2 receptor-specific monoclonal antibody LO-Tact-1 with cyclosporin A and steroids in renal transplantation.

Hiesse C; Kriaa F; Alard P; Lantz O; Noury J; Bensadoun H; Benoit G; Charpentier B; Fries D; Bazin H

Department of Nephrology, Hopital de Bicetre, Universite Paris-Sud, Paris, France.

Transplant international - official journal of the European Society for Organ Transplantation (Germany) 1992, 5 Suppl 1 pS444-7, ISSN 0934-0874--Print Journal Code: 8908516

Publishing Model Print

Document type: Clinical Trial; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

LO-Tact-1 is a rat anti-human monoclonal antibody which is directed to the 55-kDa alpha-chain of the interleukin 2 (IL2) receptor. We conducted a pilot trial in 15 first-time cadaveric renal transplant patients undergoing for immunosuppression a 14-day course of LO-Tact-1 (10 mg i.v. daily) together with cyclosporine, low dose steroids (0.5 mg/kg) and azathioprine. Results showed a good immunosuppressive effect, as measured by the similar incidence of acute rejection episodes (0.6 per patient) when compared with 20 patients treated during the same period with our standard quadruple prophylactic combination with higher initial doses of steroids (2 mg/kg) and antilymphocyte globulin (ALG) instead of LO-Tact-1 (0.4 per patient). At 2 years post-transplant, graft survival was 93%, and only 1 patient lost his kidney by rejection. No local or general adverse effect of antibody administration was encountered, and haematological changes remained of minor importance. Local bacterial infection was observed in 3 patients, but viral diseases (including cytomegalovirus, CMV) remained exceptional. In contrast, severe clinical CMV infections occurred in 3 patients (15%) treated by ALG. Nine of 15 patients developed rat-specific antibodies, but only 4 before the completion of LO-Tact-1 treatment, without any correlation with the further development of acute rejection. Patients who suffered rejection had lower LO-Tact-1 levels and higher soluble IL2 receptor levels during the period of infusion, suggesting the crucial importance of pharmacokinetic monitoring to adjust individual doses.

Descriptors: *Adrenal Cortex Hormones--therapeutic use--TU; *Antibodies, Monoclonal--biosynthesis--BI; *Cyclosporine--therapeutic use--TU; *Graft Rejection--epidemiology--EP; *Immunosuppressive Agents--therapeutic use--TU; *Kidney Transplantation--immunology--IM; *Receptors, Interleukin-2--immunology--IM; Animals; Antibodies, Monoclonal--drug effects--DE; Comparative Study; Drug Therapy, Combination; Graft Survival--drug effects--DE; Infection--epidemiology--EP; Kidney Transplantation--mortality--MO; Postoperative Complications--classification--CL; Postoperative Complications--epidemiology--EP; Probability; Rats; Survival Rate; Time Factors

CAS Registry No.: 0 (Adrenal Cortex Hormones); 0 (Antibodies, Monoclonal); 0 (Immunosuppressive Agents); 0 (Receptors, Interleukin-2); 59865-13-3 (Cyclosporine)

Record Date Created: 20031118

Record Date Completed: 20031223

12/9/3 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0007807539 BIOSIS NO.: 199192053310

T CELL RECEPTOR-CD3 AND CD28 USE DISTINCT INTRACELLULAR SIGNALING PATHWAYS

AUTHOR: VAN LIER R A (Reprint); BROUWER M; DE GROOT E; KRAMER I; AARDEN L A ; VERHOEVEN A J

AUTHOR ADDRESS: C/O PUBLICATION SECTETARIAT, CENTRAL LAB, NETHERLANDS RED CROSS BLOOD TRANSFUSION SERVICE, PO BOX 9406, NL-1006 AK AMSTERDAM, NETHERLANDS**NETHERLANDS

JOURNAL: European Journal of Immunology 21 (7): p1775-1778 1991
ISSN: 0014-2980
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Ligation of the T cell membrane antigen CD28 strongly enhances cytokine secretion in human T lymphocytes that are activated via T cell receptor (TcR)/CD3 or CD2 molecules. This study was undertaken to investigate whether, as has been indicated for activation via TcR/CD3, stimulation via CD28 is dependent on the activation of protein kinase C (PKC). Two inhibitors of PKC, 1-alkyl 2-methyl-glycerol and staurosporine, caused a dose-dependent inhibition of T cell proliferation induced by anti-CD3 monoclonal antibodies (mAb). The induction of interleukin (IL) 2 secretion was found to be more sensitive to the effects of the PKC inhibitors than the up-regulation of IL 2 receptor expression. In marked contrast, the anti-CD28 mAb-mediated enhancement of T cell proliferation and IL 2 secretion were insensitive to the action of either compound. We conclude that two independent signaling pathways may be operational in human T cells. The first used by TcR/CD3 depends on the activation of PKC, whereas the second is employed by CD28 and functions independently of PKC.

REGISTRY NUMBERS: 141436-78-4: PROTEIN KINASE C

DESCRIPTORS: HUMAN MONOCLONAL ANTIBODY PROTEIN KINASE C INTERLEUKIN 2

SECRETION T CELL PROLIFERATION

DESCRIPTORS:

MAJOR CONCEPTS: Blood and Lymphatics--Transport and Circulation; Cell Biology; Clinical Endocrinology--Human Medicine, Medical Sciences; Development; Endocrine System--Chemical Coordination and Homeostasis; Enzymology--Biochemistry and Molecular Biophysics; Membranes--Cell Biology; Metabolism

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

CHEMICALS & BIOCHEMICALS: PROTEIN KINASE C

CONCEPT CODES:

02508 Cytology - Human
10064 Biochemistry studies - Proteins, peptides and amino acids
10068 Biochemistry studies - Carbohydrates
10508 Biophysics - Membrane phenomena
10808 Enzymes - Physiological studies
13004 Metabolism - Carbohydrates
13012 Metabolism - Proteins, peptides and amino acids
15004 Blood - Blood cell studies
15008 Blood - Lymphatic tissue and reticuloendothelial system
17002 Endocrine - General
25508 Development and Embryology - Morphogenesis
34508 Immunology - Immunopathology, tissue immunology

BIOSYSTEMATIC CODES:

86215 Hominidae

12/9/4 (Item 2 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0007807446 BIOSIS NO.: 199192053217

THE EFFECTS OF BLOCKADE OF INTERLEUKIN 2 RECEPTORS AND INTERLEUKIN 4

RECEPTORS ON CYTOKINE PRODUCTION

AUTHOR: LAI K N (Reprint); LEUNG J C K; LI P K T; LARCHE M; RITTER M A

AUTHOR ADDRESS: CHIN UNIV HONG KONG, SHATIN, HONG KONG**HONG KONG

JOURNAL: APMIS 99 (5): p434-442 1991

ISSN: 0903-4641

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: The understanding of the regulation of cytokine production and T-cell proliferation by other cytokines is far from complete. We have examined the supernatant concentration of different cytokines in cultured peripheral blood lymphocytes (PBL) incubated with monoclonal antibodies against the interleukin-2 receptor (IL-2R) or interleukin-4 receptor (IL-4R) complex in order to analyse the importance of these receptors in the production of other cytokines. The PBL cultures were stimulated with phytohaemagglutinin and phorbol myristate acetate. The addition of anti-Tac to PBL cultures resulted in increased free IL-2 due to blockade of IL-2R. MR6 (a monoclonal antibody against IL-4R) did not affect the supernatant concentration of IL-2 in cultured PBL. Blockade of IL-2R or IL-4R both resulted in increased IL-4 in supernatant. The increase in supernatant concentration of IL-4 in PBL cultured with MR6 was due to a direct interaction with the IL-4R complex but the increase in IL-4 with anti-Tac was due to the accumulation of free IL-4 as an effective blockade of IL-2R prevented the full expression of IL-4R. Neither anti-Tac nor MR6 affected the IL-6 production by activated PBL, suggesting the existence of an IL-2- and IL-4-independent pathway. Blockade of IL-2R or IL-4R both resulted in a reduction of interferon-gamma (IFN-gamma) production, indicating that both endogenously generated IL-2 and IL-4 are important mediators of IFN-gamma induction in PBL cultures stimulated with T-cell mitogens.

DESCRIPTORS: HUMAN MONOCLONAL ANTIBODY PERIPHERAL BLOOD LYMPHOCYTE

INTERFERON GAMMA PRODUCTION

DESCRIPTORS:

MAJOR CONCEPTS: Blood and Lymphatics--Transport and Circulation; Cell Biology; Clinical Endocrinology--Human Medicine, Medical Sciences; Endocrine System--Chemical Coordination and Homeostasis; Membranes--Cell Biology; Metabolism

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

CONCEPT CODES:

02508 Cytology - Human

10064 Biochemistry studies - Proteins, peptides and amino acids

10068 Biochemistry studies - Carbohydrates

10508 Biophysics - Membrane phenomena

13012 Metabolism - Proteins, peptides and amino acids

15002 Blood - Blood and lymph studies

15004 Blood - Blood cell studies

15008 Blood - Lymphatic tissue and reticuloendothelial system

17002 Endocrine - General

34508 Immunology - Immunopathology, tissue immunology

BIOSYSTEMATIC CODES:

86215 Hominidae

12/9/5 (Item 3 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0007720783 BIOSIS NO.: 199191103674

IMMOBILIZED ANTI-CD5 TOGETHER WITH PROLONGED ACTIVATION OF PROTEIN KINASE C
INDUCE INTERLEUKIN 2-DEPENDENT T CELL GROWTH EVIDENCE FOR SIGNAL
TRANSDUCTION THROUGH CD5

AUTHOR: VANDENBERGHE P (Reprint); CEUPPENS J L

AUTHOR ADDRESS: LAB CLIN IMMUNOL, UNIV HOSP ST-RAFAEL, KAPUCIJNENVOER 33,
B-3000 LEUVEN, BELG**BELGIUM

JOURNAL: European Journal of Immunology 21 (2): p251-260 1991

ISSN: 0014-2980

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: Monoclonal antibodies (mAb) identifying the CD5 antigen were used to stimulate human peripheral blood T lymphocytes. Three out of three anti-CD5 mAb, 10.2, OKT1 and anti-Leu-1 induced vigorous proliferation of purified T cells in the presence of 1.6 nM phorbol 12-myristate 13-acetate (PMA). Immobilization of anti-CD5 mAb on a solid support was necessary for the induction of a proliferative response. Neither 1.6 nM PMA, nor immobilized anti-CD5 mAb were mitogenic as a sole stimulus. mAb identifying CD4, CD7, CD11a, CD18, and major histocompatibility complex class I molecules were not comitogenic with PMA. Anti-CD5/PMA-induced cell proliferation proceeded by an interleukin 2 (IL 2)-dependent mechanism, as was demonstrated by the cell surface expression of the p55 chain of the IL 2 receptor (IL 2R), the production of IL 2 and the inhibition of the proliferative response by anti-IL 2R mAb anti-Tac. There was no strict requirement for detectable numbers of monocytes, although cell proliferation could be enhanced by the monocyte-derived cytokines IL 1 and IL 6. Phorbol 12,13-dibutyrate and mezerein could substitute for PMA in this activation pathway, but synthetic diacylglycerols and phorbol esters that do not activate protein kinase C (PKC) could not, indicating a need for prolonged activation of PKC. T cells activated by anti-CD5/PMA are sensitive to inhibition by cyclosporin A (CsA) and by prostaglandin E2 (PGE2). This contrasts with anti-CD28/PMA-induced T cell proliferation, which is resistant to CsA and PGE2. Cell surface expression of CD5 was strongly up-regulated by PMA, whereas CD3 expression was down-regulated. We conclude that T cell activation can be triggered by engagement of CD5 by immobilized anti-CD5 mAb, combined with prolonged activation of PKC. These data support a role for CD5 as an independent signal transducing molecule.

REGISTRY NUMBERS: 141436-78-4: PROTEIN KINASE C

DESCRIPTORS: HUMAN MONOCLONAL ANTIBODY MAJOR HISTOCOMPATIBILITY COMPLEX T
LYMPHOCYTE

DESCRIPTORS:

MAJOR CONCEPTS: Blood and Lymphatics--Transport and Circulation; Cell
Biology; Clinical Endocrinology--Human Medicine, Medical Sciences;
Endocrine System--Chemical Coordination and Homeostasis; Enzymology--
Biochemistry and Molecular Biophysics; Metabolism

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata,
Animalia

COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates;
Vertebrates

CHEMICALS & BIOCHEMICALS: PROTEIN KINASE C

CONCEPT CODES:

02508 Cytology - Human

03508 Genetics - Human

10064 Biochemistry studies - Proteins, peptides and amino acids

10068 Biochemistry studies - Carbohydrates
10808 Enzymes - Physiological studies
13004 Metabolism - Carbohydrates
13012 Metabolism - Proteins, peptides and amino acids
15008 Blood - Lymphatic tissue and reticuloendothelial system
17002 Endocrine - General
34502 Immunology - General and methods
34508 Immunology - Immunopathology, tissue immunology
BIOSYSTEMATIC CODES:
86215 Hominidae

12/9/6 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0007656501 BIOSIS NO.: 199191039392
PRODUCTION OF INTERLEUKIN-2 BY YAC-1 CELLS STIMULATED WITH INTERLEUKIN-1
AND ITS AUGMENTATION OF THE NATURAL KILLER ACTIVITY
AUTHOR: SUZUKI Y (Reprint); DAIMARU O; NOTAKE K; YOKOCHI T
AUTHOR ADDRESS: DEP MICROBIOLOGY, AICHI MEDICAL UNIVERSITY SCH MED,
NAGAKUTE, AICHI 480-11, JAPAN**JAPAN
JOURNAL: Immunology Letters 26 (3): p239-244 1990
ISSN: 0165-2478
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The production of interleukin-2 (IL-2) by YAC-1 cells stimulated with interleukin-1 (IL-1) was examined in the in vitro culture system. The IL-2 activity was detectable in the culture supernatant of YAC-1 cells stimulated with either a mouse IL-1 preparation or human purified IL-1. This activity could be detected 1 h after stimulation with IL-1. The addition of monoclonal antibody reactive with mouse IL-2 receptor completely blocked the IL-2 activity in the culture supernatant of IL-1-stimulated YAC-1 cells. Further, the culture supernatant of IL-1-stimulated YAC-1 cells augmented the NK activity in mouse spleen cells. The role of the IL-2 activity in the culture supernatant of IL-1-stimulated YAC-1 cells on augmentation of the NK activity is discussed.

DESCRIPTORS: MOUSE HUMAN MONOCLONAL ANTIBODY INTERLEUKIN-2 RECEPTOR
SPLENOCYTES
DESCRIPTORS:

MAJOR CONCEPTS: Blood and Lymphatics--Transport and Circulation; Cell Biology; Clinical Endocrinology--Human Medicine, Medical Sciences; Endocrine System--Chemical Coordination and Homeostasis; Immune System --Chemical Coordination and Homeostasis; Membranes--Cell Biology; Metabolism

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia

COMMON TAXONOMIC TERMS: Humans; Primates; Animals; Chordates; Mammals; Nonhuman Vertebrates; Nonhuman Mammals; Rodents; Vertebrates

CONCEPT CODES:

02506 Cytology - Animal
10064 Biochemistry studies - Proteins, peptides and amino acids
10068 Biochemistry studies - Carbohydrates
10508 Biophysics - Membrane phenomena
13004 Metabolism - Carbohydrates
13012 Metabolism - Proteins, peptides and amino acids

15008 Blood - Lymphatic tissue and reticuloendothelial system
17002 Endocrine - General
34502 Immunology - General and methods
34508 Immunology - Immunopathology, tissue immunology

BIOSYSTEMATIC CODES:

86215 Hominidae
86375 Muridae

12/9/7 (Item 5 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0007302962 BIOSIS NO.: 199090087441

**PNEUMONITIS IN BONE MARROW TRANSPLANT RECIPIENTS RESULTS FROM A LOCAL
IMMUNE RESPONSE**

AUTHOR: MILBURN H J (Reprint); DU BOIS R M; PRENTICE H G; POULTER L W

AUTHOR ADDRESS: DEP RESPIRATORY MED, GUY'S HOSP, ST THOMAS ST, LONDON SE1,
ENGLAND, UK**UK

JOURNAL: Clinical and Experimental Immunology 81 (2): p232-237 1990

ISSN: 0009-9104

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: Eighteen recipients of allogeneic T cell-depleted bone marrow who developed 22 episodes of interstitial pneumonitis were investigated by bronchoalveolar lavage for the cause of pneumonitis. The cells obtained were examined using a panel of monoclonal antibodies with immunocytochemical techniques to identify lymphocyte subsets and the presence of surface molecules indicative of lymphocyte activation. The majority of patients had an excess of lymphocytes in lavage and most of these cells were positively stained with the McAb recognizing the CD8 antigen (suppressor/cytotoxic type T cells). Although the proportions of CD4+ (helper type) T cells were below normal, the absolute numbers were within normal limits, thus the CD4: CD8 ratio was consistently 1: 1 or less. A large proportion of the CD8+ cells displayed HLA-DR molecules (RFDR1+), interleukin-2 (IL-2) receptors (CD25+) and high concentration of CD7 antigen (RFT2+). Further analysis revealed that most CD8+ cells were Cd5+ (RFT+) yet a large proportion (20-40%) were CD5-. A majority of CD8+ cells were also CD38+ (RFT10+) and Leu7+. No clear correlation between the emergence of a raised proportion of activated CD8+ cells and diagnosed cytomegalovirus infection was found. These results demonstrate, however, that cells with the phenotype of the resident T cells of the bronchial epithelium (CD8+ CD5-) emerge to the air spaces and express activation markers. This raises the intriguing paradox of an aggressive local immune response occurring in an otherwise immunosuppressed group of patients.

DESCRIPTORS: HUMAN MONOCLONAL ANTIBODY INTERLEUKIN-2 CD ANTIGENS T
LYMPHOCYTES BRONCHOALVEOLAR LAVAGE

DESCRIPTORS:

MAJOR CONCEPTS: Blood and Lymphatics--Transport and Circulation; Cell
Biology; Clinical Endocrinology--Human Medicine, Medical Sciences;
Endocrine System--Chemical Coordination and Homeostasis; Hematology--
Human Medicine, Medical Sciences; Pathology; Physiology; Pulmonary
Medicine--Human Medicine, Medical Sciences

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata,
Animalia

COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates;

Vertebrates

CONCEPT CODES:

02508 Cytology - Human
10064 Biochemistry studies - Proteins, peptides and amino acids
10068 Biochemistry studies - Carbohydrates
11107 Anatomy and Histology - Regeneration and transplantation
12508 Pathology - Inflammation and inflammatory disease
15004 Blood - Blood cell studies
15006 Blood - Blood, lymphatic and reticuloendothelial pathologies
15008 Blood - Lymphatic tissue and reticuloendothelial system
16001 Respiratory system - General and methods
16006 Respiratory system - Pathology
17002 Endocrine - General
34502 Immunology - General and methods
34508 Immunology - Immunopathology, tissue immunology

BIOSYSTEMATIC CODES:

86215 Hominidae

12/9/8 (Item 6 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0007198097 BIOSIS NO.: 199089115988

INHIBITION BY ANTI-HLA CLASS I MAB OF IL-2 AND IL-2 RECEPTOR SYNTHESIS IN LYMPHOCYTES STIMULATED WITH PHA-P

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ABSTRACT: Inhibition by anti-HLA Class I monoclonal antibody (mAb) Q6/64 of phytohemagglutinin (PHA)-P-induced peripheral blood mononuclear cell (PBMC) proliferation is associated with a reduction of Tac expression and interleukin 2 (IL-2) secretion. To analyze the mechanism(s) underlying the latter phenomena, the Tac gene and IL-2 gene transcription was analyzed by a nuclear transcription assay. No synthesis of Tac and IL-2 mRNA was detected in PBMC stimulated with PHA-P in the presence of mAb Q6/64. In conjunction with our recently published data, these results indicate that the blocking by anti-HLA Class I mAb of PHA-P induced PBMC proliferation reflects an inhibitory effect within the signal transduction pathway leading to transcriptional activation of IL-2 and IL-2 receptor genes.

DESCRIPTORS: HUMAN MONOCLONAL ANTIBODY INTERLEUKIN 2 PHYTOHEMAGGLUTININ P TAC EXPRESSION GENE TRANSCRIPTION

DESCRIPTORS:

MAJOR CONCEPTS: Blood and Lymphatics--Transport and Circulation; Cell Biology; Clinical Endocrinology--Human Medicine, Medical Sciences; Genetics; Immune System--Chemical Coordination and Homeostasis; Metabolism; Molecular Genetics--Biochemistry and Molecular Biophysics
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

CONCEPT CODES:

02508 Cytology - Human
03508 Genetics - Human
10062 Biochemistry studies - Nucleic acids, purines and pyrimidines
10064 Biochemistry studies - Proteins, peptides and amino acids
10068 Biochemistry studies - Carbohydrates
10300 Replication, transcription, translation
13012 Metabolism - Proteins, peptides and amino acids
13014 Metabolism - Nucleic acids, purines and pyrimidines
15004 Blood - Blood cell studies
15008 Blood - Lymphatic tissue and reticuloendothelial system
34502 Immunology - General and methods
34508 Immunology - Immunopathology, tissue immunology
51522 Plant physiology - Chemical constituents
54000 Pharmacognosy and pharmaceutical botany

BIOSYSTEMATIC CODES:

86215 Hominidae

12/9/9 (Item 7 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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**SOLUBLE CD8 AG. SOLUBLE IL-2-RECEPTOR AND TNF SERUM LEVELS IN
STERIOD-RESISTANT ACUTE GVHD RELATION WITH SUBSEQUENT RESPONSE TO AN
ANTI-IL-2 RECEPTOR MOAB BB-10 TREATMENT**

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JOURNAL: Nouvelle Revue Francaise d'Hematologie 32 (3): p218 1990

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IMMUNOSUPPRESSANT-DRUG INTERLEUKIN-2 TUMOR NECROSIS FACTOR GRAFT VS. HOST
DISEASE

DESCRIPTORS:

MAJOR CONCEPTS: Clinical Endocrinology--Human Medicine, Medical Sciences;
Endocrine System--Chemical Coordination and Homeostasis; Hematology--
Human Medicine, Medical Sciences; Pharmacology

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata,
Animalia

COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates;
Vertebrates

CONCEPT CODES:

00520 General biology - Symposia, transactions and proceedings
10064 Biochemistry studies - Proteins, peptides and amino acids
10067 Biochemistry studies - Sterols and steroids
10068 Biochemistry studies - Carbohydrates
12512 Pathology - Therapy
15006 Blood - Blood, lymphatic and reticuloendothelial pathologies
17002 Endocrine - General
22005 Pharmacology - Clinical pharmacology
22018 Pharmacology - Immunological processes and allergy
34508 Immunology - Immunopathology, tissue immunology

BIOSYSTEMATIC CODES:

86215 Hominidae